

08/809723

- 1 -

## DESCRIPTION

NEW COMPOUND

## 5 TECHNICAL FIELD

The present invention relates to new polypeptide compound and a pharmaceutically acceptable salt thereof which are useful as a medicament.

## 10 BACKGROUND ART

In U.S. Pat. No. 5,376,634, there are disclosed the polypeptide compound and a pharmaceutically acceptable salt thereof, which have antimicrobial activities (especially antifungal activity).

15

## DISCLOSURE OF INVENTION

The present invention relates to new polypeptide compound and a pharmaceutically acceptable salt thereof.

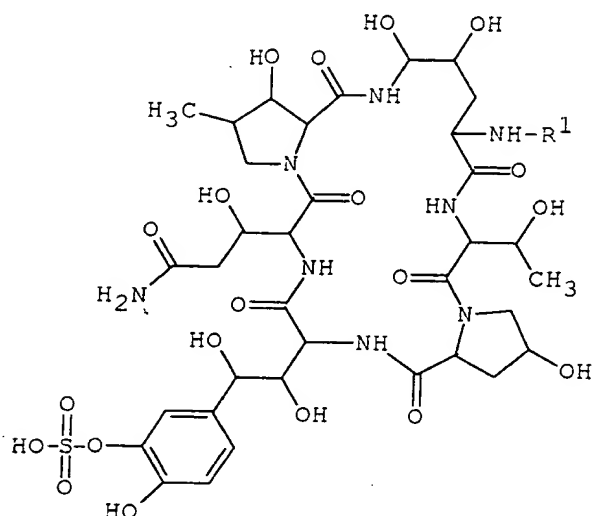
More particularly, it relates to new polypeptide  
20 compound and a pharmaceutically acceptable salt thereof, which have antimicrobial activities [especially, - antifungal activities, in which the fungi may include Aspergillus, Cryptococcus, Candida, Mucor, Actinomyces, Histoplasma, Dermatophyte, Malassezia, Fusarium and the like.], inhibitory activity on  $\beta$ -1,3-glucan synthase, and further which are expected to be useful for the prophylactic and/or therapeutic treatment of Pneumocystis carinii infection (e.g. Pneumocystis carinii pneumonia) in a human being or an animal, to a process for preparation thereof, to a pharmaceutical composition comprising the same, and to a method for the prophylactic and/or  
30 therapeutic treatment of infectious diseases including Pneumocystis carinii infection (e.g. Pneumocystis carinii pneumonia) in a human being or an animal.

35

2

08809723 05219

The object polypeptide compound used in the present invention are new and can be represented by the following general formula [I] :



[I]

wherein R<sup>1</sup> is lower alkanoyl substituted with unsaturated 6-membered heteromonocyclic group containing at least one nitrogen atom which may have one or more suitable substituent(s);

lower alkanoyl substituted with 1,2,3,4-tetrahydroisoquinoline which may have one or more suitable substituent(s);

lower alkanoyl substituted with unsaturated condensed heterocyclic group containing at least one oxygen atom which may have one or more suitable substituent(s);

lower alkanoyl substituted with unsaturated condensed heterocyclic group containing 1 to 3 sulfur atom(s) which may have one or more suitable substituent(s);

lower alkanoyl substituted with

unsaturated condensed heterocyclic group  
containing 2 or more nitrogen atom(s) which  
may have one or more suitable  
substituent(s);

5

lower alkanoyl substituted with saturated  
3 to 8 membered heteromonocyclic group  
containing at least one nitrogen atom which  
may have one or more suitable  
substituent(s);

10

ar(lower)alkenoyl substituted with aryl  
which may have one or more suitable  
substituent(s);

\* ~~naphthyl~~(lower)alkenoyl which may have one  
or more higher alkoxy;

15

lower alkynoyl which may have one or more  
suitable substituent(s);

\* (C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with naphthyl  
having higher alkoxy;

20

ar(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl  
having one or more suitable substituent(s),  
in which ar(C<sub>2</sub>-C<sub>6</sub>)alkanoyl may have one or  
more suitable substituent(s);

25

aroyl substituted with heterocyclic group  
which may have one or more suitable  
substituent(s), in which aroyl may have one  
or more suitable substituent(s);

30

aroyl substituted with aryl having  
heterocyclic(higher)alkoxy, in which  
heterocyclic group may have one or more  
suitable substituent(s);

aroyl substituted with aryl having lower  
alkoxy(higher)alkoxy;

aroyl substituted with aryl having lower  
alkenyl(lower)alkoxy;

35

aroyl substituted with 2 lower alkoxy;

A

08809723.052197  
167250" E220880

aroyl substituted with aryl having higher alkyl;

ar(lower)alkoxy(lower)alkanoyl which may have one or more suitable substituent(s);

lower alkanoyl substituted with pyrazolyl  
which has lower alkyl and aryl having higher  
alkoxy;

aryl substituted with aryl having heterocyclicoxy, in which heterocyclicoxy may have one or more suitable substituent(s);

indolylcarbonyl having higher alkyl;

naphthoyl having lower alkyl;

naphthoyl having higher alkyl;

naphthoyl having lower  
alkoxy(higher)alkoxy;

aryloxy substituted with aryl having lower  
alkoxy(lower)alkoxy(higher)alkoxy;

aroyl substituted with aryl having lower  
alkoxy(lower)alkoxy;

aryyl substituted with aryl which has aryl  
having lower alkoxy;

aroyl substituted with aryl which has aryl  
having lower alkoxy(lower)alkoxy;



aroyl substituted with aryl having  
heterocyclicoxy(higher)alkoxy;

aroyl substituted with aryl having  
aryloxy(lower)alkoxy;

5

aroyl substituted with aryl having  
heterocycliccarbonyl(higher)alkoxy;

lower alkanoyl substituted with oxazolyl  
which has aryl having higher alkoxy;

10

lower alkanoyl substituted with furyl  
which has aryl substituted with aryl having  
lower alkoxy;

lower alkanoyl substituted with triazolyl  
which has oxo and aryl having higher alkyl;

15

higher alkanoyl having hydroxy;

higher alkanoyl having ar(lower)alkyl and  
hydroxy;

3-methyl-tridecenoyl; or

20

(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl  
having higher alkoxy, in which (C<sub>2</sub>-  
C<sub>6</sub>)alkanoyl may have amino or protected  
amino.

The new polypeptide compound [I] and a  
pharmaceutically acceptable salt thereof can be prepared  
by the process as illustrated in the following reaction  
scheme or can be prepared by elimination reaction of amino  
protective group in R<sup>1</sup>.

30

35

6



wherein R<sup>1</sup> is as defined above.

Suitable pharmaceutically acceptable salts of the object polypeptide compound [I] are conventional non-toxic salts and may include a salt with a base or an acid addition salt such as a salt with an inorganic base, for example, an alkali metal salt (e.g., sodium salt, potassium salt, etc.), an alkaline earth metal salt (e.g., calcium salt, magnesium salt, etc.), an ammonium salt; a salt with an organic base, for example, an organic amine salt (e.g., triethylamine salt, pyridine salt, picoline salt, ethanolamine salt, triethanolamine salt, dicyclohexylamine salt, N,N'-dibenzylethylenediamine salt, etc.); an inorganic acid addition salt (e.g., hydrochloride, hydrobromide, sulfate, phosphate, etc.); an organic carboxylic sulfonic acid addition salt (e.g., formate, acetate, trifluoroacetate, maleate, tartrate, fumarate, methanesulfonate, benzenesulfonate, toluenesulfonate, etc.); a salt with a basic or acidic amino acid (e.g., arginine, aspartic acid, glutamic acid, etc.).

In the above and subsequent descriptions of the present specification, suitable examples and illustration of the various definitions which the present invention intends to include within the scope thereof are explained in detail as follows.

The term "lower" is used to intend a group having 1 to 6 carbon atom(s), unless otherwise provided.

The term "higher" is used to intend a group having 7 to 20 carbon atoms, unless otherwise provided.

Suitable example of "one or more" may be the number of 1 to 6, in which the preferred one may be the number of 1 to 3.

Suitable example of "lower alkanoyl" may include

8

straight or branched one such as formyl, acetyl, 2-methylacetyl, 2,2-dimethylacetyl, propionyl, butyryl, isobutyryl, pentanoyl, 2,2-dimethylpropionyl, hexanoyl, and the like.

5        Suitable example of "suitable substituent(s)" in the groups such as "lower alkanoyl substituted with unsaturated 6-membered heteromonocyclic group containing at least one nitrogen atom which may have one or more  
10       suitable substituent(s)", "lower alkanoyl substituted with 1,2,3,4-tetrahydroisoquinoline which may have one or more suitable substituent(s)", etc. may include lower alkoxy as mentioned below, higher alkoxy as mentioned below, lower alkyl as mentioned below, higher alkyl as mentioned below, higher alkoxy(lower)alkyl, lower alkoxycarbonyl, oxo, aryl  
15       which may have one or more lower alkoxy, aryl which may have one or more higher alkoxy, aryl which may have one or more lower alkyl, aryl which may have one or more higher alkyl, aryl substituted with aryl which may have one or more lower alkoxy, aryl substituted with aryl which may  
20       have one or more higher alkoxy, aryl substituted with aryl which may have one or more lower alkyl, aryl substituted with aryl which may have one or more higher alkyl, aroyl which may have one or more lower alkoxy, aroyl which may have one or more higher alkoxy, aroyl which may have one  
25       or more lower alkyl, aroyl which may have one or more higher alkyl, heterocyclic group which may have one or more lower alkoxy, heterocyclic group which may have one or more higher alkoxy, aryl having heterocyclic(higher)alkoxy, heterocyclic group which may  
30       have aryl having higher alkoxy, heterocyclic group which may have aryl having lower alkoxy(higher)alkoxy, heterocyclic group which may have aryl having lower alkoxy, lower alkoxy(lower)alkyl, halo(lower)alkoxy, lower alkenyloxy, halo(higher)alkoxy, lower  
35       alkoxy(higher)alkoxy, aryl which may have one or more

9

08009723 052147  
467250 82460880

lower alkoxy(lower)alkoxy, heterocyclic group, aryl which may have one or more lower alkoxy(higher)alkoxy, aryl which may have one or more higher alkenyloxy, cyclo(lower)alkyl which may have aryl, aryl substituted with heterocyclic group which may have lower alkyl and oxo, cyclo(lower)alkyl which may have one or more lower alkyl, aryl which may have cyclo(lower)alkyl, aryl which may have heterocyclic group, and the like.

Suitable example of "lower alkoxy" may include straight or branched one such as methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, tert-butoxy, pentyloxy, tert-pentyloxy, neo-pentyloxy, hexyloxy, isohexyloxy and the like,

in which the preferred one may be methoxy, ethoxy, propoxy, butoxy, pentyloxy, hexyloxy and isohexyloxy.

Suitable example of "higher alkoxy" may include straight or branched one such as heptyloxy, octyloxy, 3,5-dimethyloctyloxy, 3,7-dimethyloctyloxy, nonyloxy, decyloxy, undecyloxy, dodecyloxy, tridecyloxy, tetradecyloxy, hexadecyloxy, heptadecyloxy, octadecyloxy, nonadecyloxy, icosyloxy, and the like,

in which the preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the more preferred one may be heptyloxy and octyloxy.

Suitable example of "lower alkyl" may include straight or branched one having 1 to 6 carbon atom(s), such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, tert-pentyl, neo-pentyl, hexyl, isohexyl and the like,

in which the preferred one may be methyl, pentyl, hexyl and isohexyl.

Suitable example of "higher alkyl" may include straight or branched one having 7 to 20 carbon atoms, such as heptyl, octyl, 3,5-dimethyloctyl, 3,7-dimethyloctyl, nonyl, decyl, undecyl, dodecyl, tridecyl, tetradecyl, pentadecyl, hexadecyl, heptadecyl, octadecyl, nonadecyl,

icosyl, and the like,

in which the preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkyl, and the more preferred one may be heptyl, octyl, nonyl and decyl.

Suitable example of "aryl" and "ar" moiety may  
5 include phenyl which may have lower alkyl (e.g., phenyl, mesityl, tolyl, etc.), naphthyl, anthryl, and the like, in which the preferred one may be phenyl and naphthyl.

Suitable example of "aroyl" may include benzoyl, toluoyl, naphthoyl, anthrylcarbonyl, and the like,  
10 in which the preferred one may be benzoyl and naphthoyl.

Suitable example of "heterocyclic group" and "heterocyclic" moiety may include

unsaturated 3 to 8-membered (more preferably 5 or 6-  
15 membered) heteromonocyclic group containing 1 to 4 nitrogen atom(s), for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, dihydropyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl (e.g., 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, etc.),  
20 tetrazolyl (e.g., 1H-tetrazolyl, 2H-tetrazolyl, etc.), etc.;

saturated 3 to 8-membered (more preferably 5 or 6-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s), for example, pyrrolidinyl, imidazolidinyl,  
25 piperidyl, piperazinyl, etc.;

unsaturated condensed heterocyclic group containing 1 to 4 nitrogen atom(s), for example, indolyl, isoindolyl, indolinyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl, etc.;

30 unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, oxazolyl, isoxazolyl, oxadiazolyl (e.g., 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, etc.),  
35 etc.;

//

08809723 052197 67250 2260880

saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, morpholinyl, sydnonyl, etc.;

5       unsaturated condensed heterocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, benzoxazolyl, benzoxadiazolyl, etc.;

10       unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, thiazolyl, isothiazolyl, thiadiazolyl (e.g., 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.), dihydrothiazinyl, etc.;

15       saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, thiazolidinyl, etc.;

20       unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 sulfur atom(s), for example, thienyl, dihydrodithiynyl, dihydrodithionyl, etc.;

      unsaturated condensed heterocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, benzothiazolyl, benzothiadiazolyl, etc.;

25       unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom, for example, furyl, etc.;

30       saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom, for example, tetrahydrofuran, tetrahydropyran, etc.;

      unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom and 1 to 2 sulfur atom(s), for example, dihydrooxathiinyl, etc.;

35       unsaturated condensed heterocyclic group containing 1

12

08809723 052197

to 2 sulfur atom(s), for example, benzothienyl, benzodithiiny, etc.;

unsaturated condensed heterocyclic group containing an oxygen atom and 1 to 2 sulfur atom(s), for example, 5 benzoxathiiny, etc.; and the like.

Suitable example of "halo" may include fluoro, chloro, bromo and iodo.

10 Suitable example of "lower alkenyloxy" may include vinyloxy, 1-(or 2-)propenyloxy, 1-(or 2- or 3-)butenyloxy, 1-(or 2- or 3- or 4-)pentyloxy, 1-(or 2- or 3- or 4- or 5-)hexenyloxy, and the like, in which the preferred one may be (C<sub>2</sub>-C<sub>6</sub>)alkenyloxy, and the most preferred one may be 5-hexenyloxy.

15 Suitable example of "higher alkenyloxy" may include (C<sub>7</sub>-C<sub>20</sub>)alkenyloxy, in which the preferred one may be 6-heptenyloxy and 7-octenyloxy.

20 Suitable example of "cyclo(lower)alkyl" may include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and the like, in which the preferred one may be cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyl, and the most preferred one may be cyclohexyl.

Suitable example of "higher alkanoyl" may include heptanoyl, octanoyl, nonanoyl, decanoyl, undecanoyl, lauroyl, tridecanoyl, tetradecanoyl, pentadecanoyl, 25 hexadecanoyl, heptadecanoyl, octadecanoyl, nonadecanoyl, icosanoyl, and the like, in which the preferred one may be (C<sub>7</sub>-C<sub>20</sub>)alkanoyl, and the most preferred one may be hexadecanoyl.

30 Suitable example of "ar(lower)alkyl" may include benzyl, phenethyl, phenylpropyl, phenylbutyl, phenylpentyl, phenylhexyl, naphthylmethyl, naphthylethyl, naphthylpropyl, naphthylbutyl, naphthylpentyl, naphthylhexyl, and the like, in which the preferred one may be phenyl(C<sub>1</sub>-C<sub>4</sub>)alkyl, and the most preferred one may 35 be benzyl.



Suitable example of "protected amino" may include lower or higher alkoxycarbonylamino (e.g., methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, t-pentyloxycarbonylamino, heptyloxycarbonylamino, etc.), ar(lower)alkoxycarbonylamino [e.g., phenyl(lower)alkoxycarbonylamino (e.g., benzyloxycarbonylamino, etc.), etc.], an amino group substituted with a conventional protecting group such as ar(lower)alkyl which may have suitable substituent(s) (e.g., benzyl, trityl, etc.) and the like, in which the preferred one may be phenyl(lower)alkoxycarbonylamino, and the most preferred one may be benzyloxycarbonylamino.

Suitable example of "lower alkanoyl" in the term of "lower alkanoyl substituted with unsaturated 6-membered heteromonocyclic group containing at least one nitrogen atom which may have one or more suitable substituent(s)" can be referred to aforementioned "lower alkanoyl", in which the preferred one may be (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, and the more preferred one may be formyl.

Suitable example of "unsaturated 6-membered heteromonocyclic group containing at least one nitrogen atom" in the term of "lower alkanoyl substituted with unsaturated 6-membered heteromonocyclic group containing at least one nitrogen atom which may have one or more suitable substituent(s)" may include pyridyl, dihydropyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazinyl (e.g., 4H-1,2,4-triazinyl, 1H-1,2,3-triazinyl, etc.), tetrazinyl (e.g., 1,2,4,5-tetrazinyl, 1,2,3,4-tetrazinyl, etc.), and the like,

in which the preferred one may be unsaturated 6-membered heteromonocyclic group containing 1 to 3 nitrogen atom(s), and the most preferred one may be pyridyl and pyridazinyl.

Suitable example of "suitable substituent(s)" in the

term of "lower alkanoyl substituted with unsaturated 6-membered heteromonocyclic groups containing at least one nitrogen atom which may have one or more suitable substituent(s)" can be referred to aforementioned

5 "suitable substituent(s)",

in which the preferred one may be higher alkoxy, higher alkoxy(lower)alkyl, heterocyclic group which may have aryl having higher alkoxy, aryl which may have one or more higher alkoxy, aryl substituted with aryl which may have

10 lower alkoxy, heterocyclic group which may have aryl having lower alkoxy(higher)alkoxy, and heterocyclic group which may have aryl having lower alkoxy, and the more preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, (C<sub>7</sub>-C<sub>14</sub>)alkoxy-

15 (C<sub>1</sub>-C<sub>4</sub>)alkyl, 3 to 8-membered saturated heteromonocyclic group containing at least one nitrogen atom which may have phenyl having 1 to 3 (C<sub>7</sub>-C<sub>14</sub>)alkoxy, phenyl which may have 1 to 3 (C<sub>7</sub>-C<sub>14</sub>)alkoxy, phenyl substituted with phenyl which may have 1 to 3 (C<sub>3</sub>-C<sub>6</sub>)alkoxy, 3 to 8-membered saturated heteromonocyclic group containing at least one

20 nitrogen atom which may have phenyl having (C<sub>1</sub>-C<sub>4</sub>)-alkoxy(C<sub>7</sub>-C<sub>14</sub>)alkoxy, and 3 to 8-membered saturated heteromonocyclic group containing at least one nitrogen atom which may have phenyl having 1 to 3 (C<sub>3</sub>-C<sub>6</sub>)alkoxy, and the most preferred one may be octyloxy,

25 octyloxymethyl, piperazinyl which has phenyl having heptyloxy or octyloxy, phenyl having heptyloxy, phenyl substituted with phenyl having butoxy, piperazinyl which has phenyl having methoxyoctyloxy, and piperazinyl which has phenyl having hexyloxy.

30

Suitable example of "lower alkanoyl" in the term of "lower alkanoyl substituted with 1,2,3,4-tetrahydroisoquinoline which may have one or more suitable substituent(s)" can be referred to aforementioned "lower

35

alkanoyl",

in which the preferred one may be (C<sub>1</sub>-C<sub>4</sub>)-alkanoyl, and the more preferred one may be formyl.

Suitable example of "suitable substituent(s)" in the term of "lower alkanoyl substituted with 1,2,3,4-tetrahydroisoquinoline which may have one or more suitable substituent(s)." can be referred to aforementioned "suitable substituent(s)",

in which the preferred one may be lower alkoxy, higher alkoxy, lower alkyl, higher alkyl and lower alkoxycarbonyl, and the more preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy and (C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl, and the most preferred one may be octyloxy and tert-butoxycarbonyl.

Suitable example of "lower alkanoyl" in the term of "lower alkanoyl substituted with unsaturated condensed heterocyclic group containing at least one oxygen atom which may have one or more suitable substituent(s)" can be referred to aforementioned "lower alkanoyl",

in which the preferred one may be (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, and the more preferred one may be formyl.

Suitable example of "unsaturated condensed heterocyclic group containing at least one oxygen atom" in the term of "lower alkanoyl substituted with unsaturated condensed heterocyclic group containing at least one oxygen atom which may have one or more suitable substituent(s)" may include unsaturated condensed heterocyclic group containing one or more oxygen atom(s) and, optionally, another hetero atom(s) except oxygen atom,

in which the preferred one may be unsaturated condensed heterocyclic group containing 1 to 3 oxygen atom(s), unsaturated condensed heterocyclic group containing 1 to 2 oxygen atom(s) and 1 to 2 sulfur atom(s) and unsaturated condensed heterocyclic group 1 to 3 oxygen atom(s) and 1 to 3 nitrogen atom(s), and the more preferred one may be

08809723 052197

benzo[b]furanyl, isobenzofuranyl, chromenyl, xanthenyl, benzoxazolyl, benzoxadiazolyl, dihydrooxathiinyl, phenoxathiinyl, and the like, and the most preferred one may be benzo[b]furanyl, chromenyl and benzoxazolyl.

5        Suitable example of "suitable substituent(s)" in the term of "lower alkanoyl substituted with unsaturated condensed heterocyclic group containing at least one oxygen atom which may have one or more suitable substituent(s)" can be referred to aforementioned

10        "suitable substituent(s)",

in which the preferred one may be lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, oxo, aryl which may have one or more lower alkoxy, heterocyclic group which may have one or more higher alkoxy, and aryl substituted with aryl which may have one or more lower alkyl, and the more preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, (C<sub>1</sub>-C<sub>4</sub>)alkyl, (C<sub>7</sub>-C<sub>14</sub>)alkyl, oxo, phenyl which may have 1 to 3 (C<sub>3</sub>-C<sub>6</sub>)alkoxy, unsaturated 6-membered heteromonochclic group containing at least one nitrogen atom which may have 1 to 3 (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and phenyl substituted with phenyl which may have 1 to 3 (C<sub>3</sub>-C<sub>6</sub>)alkyl, and the most preferred one may be octyloxy, methyl, nonyl, oxo, phenyl having hexyloxy, pyridyl having octyloxy, and phenyl substituted with phenyl having hexyl.

25        Suitable example of "lower alkanoyl" in the term of "lower alkanoyl substituted with unsaturated condensed heterocyclic group containing 1 to 3 sulfur atom(s) which may have one or more suitable substituent(s)" can be referred to aforementioned "lower alkanoyl",

30        in which the preferred one may be (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, and the more preferred one may be formyl.

Suitable example of "unsaturated condensed heterocyclic group containing 1 to 3 sulfur atom(s)" in the term of "lower alkanoyl substituted with unsaturated

17

08809723-05219

condensed heterocyclic group containing 1 to 3 sulfur atom(s) which may have one or more suitable substituent(s)" may include unsaturated condensed heterocyclic group containing only 1 to 3 sulfur atom(s),  
5 in which the preferred one may be benzothienyl and benzodithienyl, and the most preferred one may be benzothienyl.

Suitable example of "suitable substituent(s)" in the term of "lower alkanoyl substituted with unsaturated condensed heterocyclic group containing 1 to 3 sulfur atom(s) which may have one or more suitable substituent(s)" can be referred to aforementioned "suitable substituent(s)",  
10

in which the preferred one may be lower alkoxy, higher alkoxy, lower alkyl and higher alkyl, and more preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the most preferred one may be octyloxy.  
15

Suitable example of "lower alkanoyl" in the term of "lower alkanoyl substituted with unsaturated condensed heterocyclic group containing 2 or more nitrogen atom(s) which may have one or more suitable substituent(s)" can be referred to aforementioned "lower alkanoyl",  
20

in which the preferred one may be (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, and the most preferred one may be formyl.  
25

Suitable example of "unsaturated condensed heterocyclic group containing 2 or more nitrogen atom(s)" in the term of "lower alkanoyl substituted with unsaturated condensed heterocyclic group containing 2 or more nitrogen atom(s) which may have one or more suitable substituent(s)" may include 1H-indazolyl, purinyl, phthalazinyl, benzoimidazolyl, naphthyridinyl, quinoxalinyl, quinazolyl, cinnolinyl, pteridinyl, and the like,  
30

in which the most preferred one may be benzoimidazolyl.  
35

Suitable example of "suitable substituent(s)" in the term of "lower alkanoyl substituted with unsaturated condensed heterocyclic group containing 2 or more nitrogen atom(s) which may have one or more suitable substituent(s)" can be referred to aforementioned

"suitable substituent(s)",  
in which the preferred one may be lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, aryl which may have one or more lower alkoxy and aryl which may have one or more higher alkoxy, and the more preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkyl and phenyl which may have 1 to 3 (C<sub>1</sub>-C<sub>6</sub>)alkoxy, and the most preferred one may be nonyl and phenyl which may have hexyloxy.

Suitable example of "lower alkanoyl" in the term of "lower alkanoyl substituted with saturated 3 to 8-membered heteromonocyclic group containing at least one nitrogen atom which may have one or more suitable substituent(s)" can be referred to aforementioned "lower alkanoyl",

in which the preferred one may be (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, and the more preferred one may be formyl.

Suitable example of "saturated 3 to 8-membered heteromonocyclic group containing at least one nitrogen atom" in the term of "lower alkanoyl substituted with saturated 3 to 8-membered heteromonocyclic group containing at least one nitrogen atom which may have one or more suitable substituent(s)" may include pyrrolidinyl, imidazolidinyl, piperidyl, piperazinyl, pyrazolidinyl, morpholinyl, thiomorpholinyl, and the like,

in which the preferred one may be piperidyl and piperazinyl.

Suitable example of "suitable substituent(s)" in the term of "lower alkanoyl substituted with saturated 3 to 8-membered heteromonocyclic group containing at least one nitrogen atom which may have one or more suitable

substituent(s)" may include lower alkoxy, higher alkoxy, higher alkoxy(lower)alkyl, lower alkyl, higher alkyl, oxo, aryl which may have one or more lower alkoxy, aryl which may have one or more higher alkoxy, 5 aryl which may have one or more lower alkyl, aryl which may have one or more higher alkyl, aroyl which may have one or more lower alkoxy, aroyl which may have one or more higher alkoxy, aroyl which may have one or more lower alkyl, 10 aroyl which may have one or more higher alkyl, and the like,

in which the preferred one may be aryl which may have one or more lower alkoxy, aryl which may have one or more higher alkoxy, 15 aroyl which may have one or more lower alkoxy and aroyl which may have one or more higher alkoxy, and the more preferred one may be aryl which may have 1 to 3 higher alkoxy and aroyl which may have 1 to 3 higher alkoxy, and the much more preferred one may be phenyl 20 which may have 1 to 3 (C<sub>7</sub>-C<sub>14</sub>)alkoxy and naphthoyl which may have 1 to 3 (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the most preferred one may be phenyl which may have octyloxy and naphthoyl which may have heptyloxy.

25 Sutable example of "ar(lower)alkenoyl" in the term of "ar(lower)alkenoyl substituted with aryl which may have one or more suitable substituent(s)" may include phenyl(lower)alkenoyl (e.g., 3-phenylacryloyl, (2- or 3- or 4-)phenyl-(2- or 3-)butenoyl, 3-phenylmethacryloyl, 30 (2- or 3- or 4- or 5-)phenyl-(2- or 3- or 4-)pentanoyl, (2- or 3- or 4- or 5- or 6-)phenyl-(2- or 3- or 4- or 5-)-hexanoyl, etc.), naphthyl(lower)alkenoyl (e.g., 3-naphthylacryloyl, (2- or 3- or 4-)naphthyl-(2- or 3-)butenoyl, (2- or 3- or 4- or 5-)naphthyl-(2- or 3- or 35 4-)pentanoyl, (2- or 3- or 4- or 5- or 6-)naphthyl-(2- or

20

08809723 052197

3- or 4- or 5-)hexanoyl, etc.), and the like,  
in which the preferred one may be 3-phenylacryloyl and 3-methyl-3-phenylacryloyl.

5        Suitable example of "suitable substituent(s)" in the term of "ar(lower)alkenoyl substituted with aryl which may have one or more suitable substituent(s)" can be referred to aforementioned "suitable substituent(s)",

10        in which the preferred one may be lower alkoxy, lower alkyl, higher alkyl, lower alkoxy(lower)alkyl, halo(lower)alkoxy, lower alkenyloxy, halo(higher)alkoxy, and lower alkoxy(higher)alkoxy and the much more preferred one may be (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>7</sub>-C<sub>14</sub>)alkyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)alkyl, halo(C<sub>3</sub>-C<sub>6</sub>)alkoxy, (C<sub>3</sub>-C<sub>6</sub>)alkenyloxy, halo(C<sub>7</sub>-C<sub>14</sub>)alkoxy, and (C<sub>1</sub>-C<sub>4</sub>)alkoxy(C<sub>7</sub>-C<sub>14</sub>)alkoxy and the most preferred one may be pentyloxy, heptyl, pentyl, methoxyhexyl, fluorohexyloxy, isohexyloxy, 5-hexenyloxy, haloheptyloxy, methoxyheptyloxy, methoxyoctyloxy, and butyloxy.

20        Suitable example of "naphthyl(lower)alkenoyl" in the term of "naphthyl(lower)alkenoyl which may have one or more higher alkoxy" may include 3-naphthylacryloyl, (2- or 3- or 4-)naphthyl-(2- or 3-)butenoyl, (2- or 3- or 4- or 5-)naphthyl-(2- or 3- or 4-)pentanoyl, (2- or 3- or 4- or 5- or 6-)naphthyl-(2- or 3- or 4- or 5-)hexanoyl, and the like,

25        in which the preferred one may be 3-naphthylacryloyl.

30        Suitable example of "lower alkynoyl" in the term of "lower alkynoyl which may have one or more suitable substituent(s)" may include 2-propynoyl, (2- or 3-)butynoyl, (2- or 3- or 4-)pentynoyl, (2- or 3- or 4- or 5-)hexynoyl, and the like, in which the preferred one may be 2-propynoyl.

35        Suitable example of "suitable substituent(s)" in the

21

08809723.05219



term of "lower alkynoyl which may have one or more suitable substituent(s)" can be referred to aforementioned "suitable substituent(s)",

5 in which the preferred one may be aryl which may have one or more lower alkoxy, aryl which may have one or more higher alkoxy, aryl substituted with aryl which may have one or more lower alkyl and aryl substituted with aryl which may have one or more higher alkyl, and the more preferred one may be aryl substituted with aryl which may  
10 have 1 to 3 lower alkyl and aryl which may have 1 to 3 higher alkoxy, and the much more preferred one may be phenyl substituted with phenyl which may have 1 to 3 (C<sub>1</sub>-C<sub>6</sub>)alkyl and phenyl which may have 1 to 3 (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the most preferred one may be phenyl  
15 substituted with phenyl which may have pentyl and naphthyl which may have heptyloxy.

Suitable example of "ar(C<sub>2</sub>-C<sub>6</sub>)alkanoyl" in the term of "ar(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl having one or  
20 more suitable substituent(s), in which ar(C<sub>2</sub>-C<sub>6</sub>)alkanoyl may have one or more suitable substituent(s)" may include phenyl(C<sub>2</sub>-C<sub>6</sub>)alkanoyl [e.g., phenylacetyl, (2- or 3-)-phenylpropanoyl, (2- or 3- or 4-)phenylbutanoyl, (2- or 3- or 4- or 5-)phenylpentanoyl, (2- or 3- or 4- or 5- or 6-)-  
25 phenylhexanoyl, etc.], naphthyl(C<sub>2</sub>-C<sub>6</sub>)alkanoyl [e.g., naphthylacetyl, (2- or 3-)naphthylpropanoyl, (2- or 3- or 4-)naphthylbutanoyl, (2- or 3- or 4- or 5-)-naphthylpentanoyl, (2- or 3- or 4- or 5- or 6-)-naphthylhexanoyl, etc.], and the like,  
30 in which the preferred one may be 2-phenylacetyl and 3-phenylpropanoyl.

Suitable example of "suitable substituent(s)" in the term of "ar(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl having one or more suitable substituent(s), in which ar(C<sub>2</sub>-C<sub>6</sub>)-  
35 alkanoyl may have one or more suitable substituent(s)" may

22

08809723.052197

include lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy(lower)alkyl, oxo, aryl having one or more lower alkoxy, aryl having one or more higher alkoxy, aryl having one or more lower alkyl, aryl having one or more higher alkyl, aryl substituted with aryl having one or more lower alkoxy, aryl substituted with aryl having one or more higher alkoxy, aryl substituted with aryl having one or more lower alkyl, aryl substituted with aryl having one or more higher alkyl, aryl having one or more lower alkoxy(lower)alkoxy and the like,

in which the preferred one may be lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, and phenyl having 1 to 3 lower alkoxy(lower)alkoxy and the much more preferred one may be (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>7</sub>-C<sub>14</sub>)alkyl and phenyl having (C<sub>1</sub>-C<sub>4</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)alkoxy and the most preferred one may be pentyloxy, pentyl, heptyl and phenyl having methoxypentyloxy.

Suitable example of "suitable substituent(s)" in the term of "in which ar(C<sub>2</sub>-C<sub>6</sub>)alkanoyl may have one or more suitable substituent(s)" may be hydroxy, oxo, amino and aforementioned "protected amino".

Suitable example of "(C<sub>2</sub>-C<sub>6</sub>)alkanoyl" in the term of "(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with naphthyl having higher alkoxy" may include acetyl, propanoyl, butanoyl, pentanoyl, hexanoyl, and the like,

in which the preferred one may be propanoyl.

Suitable example of "higher alkoxy" in the term of "(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with naphthyl having higher alkoxy" can be referred to aforementioned "higher alkoxy", in which the preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the most preferred one may be heptyloxy.

Suitable example of "aroyl" in the term of "aroyl substituted with heterocyclic group which may have one or

23

more suitable substituent(s), in which aroyl may have one or more suitable substituent(s)" may include benzoyl, toluoyl, naphthoyl, and the like, in which the preferred one may be benzoyl.

5

Suitable example of "heterocyclic group" in the term of "aroyl substituted with heterocyclic group which may have one or more suitable substituent(s), in which aroyl may have one or more suitable substituent(s)" may include  
10 unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 4 nitrogen atom(s), for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, dihydropyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl (e.g., 4H-1,2,4-  
15 triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, etc.), tetrazolyl (e.g., 1H-tetrazolyl, 2H-tetrazolyl, etc.), etc.;

saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 4  
20 nitrogen atom(s), for example, pyrrolidinyl, imidazolidinyl, piperidyl, piperazinyl, etc.;

unsaturated condensed heterocyclic group containing 1 to 4 nitrogen atom(s), for example, indolyl, isoindolyl, indolinyl, indolizinyl, benzimidazolyl, quinolyl,  
25 isoquinolyl, indazolyl, benzotriazolyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, oxazolyl, isoxazolyl, oxadiazolyl (e.g.,  
30 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, etc.), etc.;

saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example,  
35 morpholinyl, sydnonyl, etc.;

24

08809723 052197

unsaturated condensed heterocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, benzoxazolyl, benzoxadiazolyl, etc.;

5       unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, thiazolyl, isothiazolyl, thiadiazolyl (e.g., 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.),  
10       dihydrothiazinyl, etc.;

          saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, thiazolidinyl, etc.;

15       unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 sulfur atom(s), for example, thienyl, dihydrodithiynyl, dihydrodithionyl, etc.;

          unsaturated condensed heterocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, benzothiazolyl, benzothiadiazolyl, etc.;

          unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom, for example, furyl, etc.;

25       saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom, for example, tetrahydrofuran, tetrahydropyran, etc.;

          unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom and 1 to 2 sulfur atom(s), for example, dihydrooxathiinyl, etc.;

          unsaturated condensed heterocyclic group containing 1 to 2 sulfur atom(s), for example, benzothienyl, benzodithiynyl, etc.;

35       unsaturated condensed heterocyclic group containing

an oxygen atom and 1 to 2 sulfur atom(s), for example, benzoxathiinyl, etc.; and the like,

in which the preferred one may be saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s), unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s),

unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s), and

unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), and the most preferred one may be piperazinyl, isoxazolyl, oxadiazolyl, thiadiazolyl, pyrazolyl, piperidyl, oxazolyl and pyrimidyl.

Suitable example of "suitable substituent(s)" in the term of "aroyl substituted with heterocyclic group which may have one or more suitable substituent(s), in which aroyl may have one or more suitable substituent(s)", can be referred to aforementioned "suitable substituent(s)",

in which the preferred one may be aryl which may have 1 to 3 higher alkoxy, aryl which may have 1 to 3 lower alkoxy, higher alkyl, heterocyclic group, aryl which may have 1 to 3 lower alkoxy(higher)alkoxy, aryl which may have higher alkenyloxy, heterocyclic group which may have aryl having lower alkoxy, cyclo(lower)alkyl which may have aryl, aryl which may have 1 to 3 lower alkyl, aryl which may have cyclo(lower)alkyl, aryl which may have higher alkenyloxy, aryl substituted with heterocyclic group which may have lower alkyl and oxo, cyclo(lower)alkyl which may have lower alkyl, aryl substituted with aryl which may have 1 to 3 lower alkoxy, and aryl which may have heterocyclic group, and the more preferred one may be phenyl which may have 1 to 3 (C<sub>7</sub>-C<sub>14</sub>)alkoxy, phenyl which may have 1 to 3 (C<sub>3</sub>-C<sub>6</sub>)alkoxy, (C<sub>7</sub>-C<sub>14</sub>)alkyl, saturated 3

26

08809723 052197

to 8-membered heteromonocyclic group containing 1 to 4  
nitrogen atom(s), phenyl which may have 1 to 3 (C<sub>1</sub>-  
C<sub>4</sub>)alkoxy (C<sub>7</sub>-C<sub>14</sub>)alkoxy, phenyl which may have (C<sub>7</sub>-  
C<sub>14</sub>)alkenyloxy, saturated 3 to 8-membered heteromonocyclic  
5 group containing 1 to 4 nitrogen atom(s) substituted with  
phenyl having (C<sub>3</sub>-C<sub>6</sub>)alkoxy, cyclo(C<sub>3</sub>-C<sub>6</sub>)alkyl which may  
have phenyl, phenyl which may have 1 to 3 (C<sub>3</sub>-C<sub>6</sub>)alkyl,  
phenyl which may have cyclo(C<sub>3</sub>-C<sub>6</sub>)alkyl, phenyl which may  
have (C<sub>7</sub>-C<sub>14</sub>)alkenyloxy, phenyl substituted with  
10 heterocyclic group which may have (C<sub>3</sub>-C<sub>6</sub>)alkyl and oxo,  
cyclo(C<sub>3</sub>-C<sub>6</sub>)alkyl which may have (C<sub>3</sub>-C<sub>6</sub>)alkyl, phenyl  
substituted with phenyl which may have 1 to 3 (C<sub>1</sub>-  
C<sub>4</sub>)alkoxy, and phenyl which may have 3 to 8-membered  
heteromonocyclic group containing 1 to 4 nitrogen atom(s),  
15 and the most preferred one may be phenyl having octyloxy,  
phenyl having pentyloxy, phenyl having hexyloxy, heptyl,  
piperidyl, phenyl having isohexyloxy, phenyl having  
heptyloxy, phenyl having methoxyheptyloxy, phenyl having  
methoxyoctyloxy, phenyl having 6-heptenyloxy, piperidyl  
20 substituted with phenyl having hexyloxy, cyclohexyl having  
phenyl, phenyl having hexyl, phenyl having cyclohexyl,  
phenyl having 7-octenyloxy, phenyl substituted with  
triazolyl having lower alkyl and oxo, cyclohexyl having  
pentyl, phenyl having methoxyoctyloxy, nonyl, phenyl  
25 substituted with phenyl having propoxy, and phenyl having  
piperidine.

Suitable example of "suitable substituent(s)" in the  
term of "in which aroyl may have one or more suitable  
substituent(s)" may be halogen, in which the preferred one  
30 may be fluoro and chloro.

Suitable example of "aroyl" in the term of "aroyl  
substituted with aryl having heterocyclic(higher)alkoxy,  
in which heterocyclic group may have one or more suitable  
substituent(s)" may include benzoyl, toluoyl, naphthoyl,  
35

27

08809723.052197

anthrylcarbonyl and the like,

in which the preferred one may be benzoyl.

Suitable example of "heterocyclic" moiety in the term of "aroyl substituted with aryl having

5 heterocyclic(higher)alkoxy, in which heterocyclic group may have one or more suitable substituent(s)" can be referred to the ones as exemplified before for "heterocyclic group" in the term of "aroyl substituted with heterocyclic group which may have one or more  
10 suitable substituent(s)",

in which the preferred one may be unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) and saturated 3 to 8-membered heteromonocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen  
15 atom(s), and the most preferred one may be triazolyl, tetrazolyl and morpholinyl.

Suitable example of "(higher)alkoxy" moiety in the term of "aroyl substituted with aryl having heterocyclic(higher)alkoxy, in which heterocyclic group  
20 may have one or more suitable substituent(s)" can be referred to aforementioned "higher alkoxy",

in which the preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the most preferred one may be octyloxy.

Suitable example of "aryl" in the term of "aroyl substituted with aryl having heterocyclic(higher)alkoxy, in which heterocyclic group may have one or more suitable substituent(s)" can be referred to aforementioned "aryl",  
25 in which the preferred one may be phenyl.

Suitable example of "suitable substituent(s)" in the term of "in which heterocyclic group may have one or more suitable substituent(s)" may be lower alkyl, in which the  
30 preferred one may be methyl.

Suitable example of "aroyl" in the term of "aroyl substituted with aryl having lower alkoxy(higher)alkoxy"  
35

26

0809723.052197

may include benzoyl, toluoyl, naphthoyl, anthrylcarbonyl and the like,

in which the preferred one may be benzoyl.

5        Suitable example of "aryl" in the term of "aroyl substituted with aryl having lower alkoxy(higher)alkoxy" can be referred to aforementioned "aryl", in which the preferred one may be phenyl.

10        Suitable example of "lower alkoxy(higher)alkoxy" in the term of "aroyl substituted with aryl having lower alkoxy(higher)alkoxy" may be methoxyheptyloxy, methoxyoctyloxy, methoxynonyloxy, methoxydecyloxy, ethoxyheptyloxy, ethoxyoctyloxy, ethoxynonyloxy, ethoxydecyloxy, ethoxyundecyloxy, propoxyundecyloxy, butoxydodecyloxy, pentyloxytridecyloxy, 15        hexyloxytetradecyloxy, propoxyheptyloxy, propoxyoctyloxy, propoxynonyloxy, butoxydecyloxy, or the like, in which the preferred one may be (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the more preferred one may be methoxyoctyloxy.

20        Suitable example of "aroyl" in the term of "aroyl substituted with aryl having lower alkenyl(lower)alkoxy" may include benzoyl, toluoyl, naphthoyl, anthrylcarbonyl and the like, in which the preferred one may be benzoyl.

25        Suitable example of "aryl" in the term of "aroyl substituted with aryl having lower alkenyl(lower)alkoxy" can be referred to aforementioned "aryl", in which the preferred one may be phenyl.

30        Suitable example of "lower alkenyl(lower)alkoxy" in the term of "aroyl substituted with aryl having lower alkenyl(lower)alkoxy" may be vinylmethoxy, vinylethoxy, vinylpropoxy, vinylbutoxy, vinylpentyloxy, vinylhexyloxy, 1-(or 2-)propenylmethoxy, 1-(or 2-)propenylethoxy, 1-(or 2-)propenylpropoxy, 1-(or 2-)propenylbutoxy, 1-(or 2-)propenylpentyloxy, 1-(or 2-)propenylhexyloxy, 1-(or 2- or 35        propenylpentyloxy, 1-(or 2-)propenylhexyloxy, 1-(or 2- or

29

08809723-052197



3-)butenylbutoxy, 1-(or 2- or 3-)butenylhexyloxy, 1-(or 2-  
or 3- or 4-)pentenylpentyloxy, 1-(or 2- or 3- or 4-)-  
pentenylhexyloxy, 1-(or 2- or 3- or 4- or 5-)-  
hexenylbutoxy, 1-(or 2- or 3- or 4- or 5-)hexenylhexyloxy,  
5 or the like,

in which the preferred one may be (C<sub>2</sub>-C<sub>6</sub>)alkenyl(C<sub>1</sub>-  
C<sub>6</sub>)alkoxy, and the more preferred one may be  
vinylhexyloxy.

10 Suitable example of "aroyl substituted with 2 lower  
alkoxy" may include benzoyl substituted with 2 lower  
alkoxy and naphthoyl substituted with 2 lower alkoxy,  
in which the preferred one may be benzoyl substituted  
with 2 (C<sub>1</sub>-C<sub>6</sub>)alkoxy, and the most preferred one may be  
15 benzoyl substituted with 2 pentyloxy.

Suitable example of "aroyl substituted with aryl  
having lower alkyl" may include benzoyl substituted with  
phenyl having lower alkyl, benzoyl substituted with  
20 naphthyl having lower alkyl, naphthoyl substituted with  
phenyl having lower alkyl, naphthoyl substituted with  
naphthyl having lower alkyl, and the like,  
in which the preferred one may be benzoyl substituted  
with phenyl having (C<sub>1</sub>-C<sub>6</sub>)alkyl, and the most preferred  
25 one may be benzoyl substituted with phenyl having hexyl  
and benzoyl substituted with phenyl having pentyl.

Suitable example of "aroyl substituted with aryl  
having higher alkyl" may include benzoyl substituted with  
30 phenyl having higher alkyl, benzoyl substituted with  
naphthyl having higher alkyl, naphthoyl substituted with  
phenyl having higher alkyl, naphthoyl substituted with  
naphthyl having higher alkyl, and the like,  
in which the preferred one may be benzoyl substituted  
35 with phenyl having (C<sub>7</sub>-C<sub>14</sub>)alkyl, and the most preferred

30

0809723-05219  
467250-2260880

one may be benzoyl substituted with phenyl having heptyl.

Suitable example of "aryloxy" moiety in the term of "aryloxy(lower)alkanoyl which may have one or more  
5 suitable substituent(s)" may include phenoxy, mesityloxy, tolyloxy, naphthyloxy, anthryloxy, and the like, in which the preferred one may be phenoxy.

Suitable example of "lower alkanoyl" moiety in the term of "aryloxy(lower)alkanoyl which may have one or more  
10 suitable substituent(s)" can be referred to aforementioned "lower alkanoyl",

in which the preferred one may be formyl, acetyl, 2,2-dimethylacetyl, propionyl, butyryl, isobutyryl and pentanoyl, hexanoyl, and the more preferred one may be  
15 (C<sub>1</sub>-C<sub>6</sub>)alkanoyl, and the much more preferred one may be formyl, acetyl, propionyl and 2,2-dimethylacetyl.

Suitable example of "suitable substituent(s)" in the term of "aryloxy(lower)alkanoyl which may have one or more  
20 suitable substituent(s)" can be referred to aforementioned "suitable substituent(s)",

in which the preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the more preferred one may be octyloxy.

Suitable example of "ar(lower)alkoxy" moiety in the  
25 term of "ar(lower)alkoxy(lower)alkanoyl which may have one or more suitable substituent(s)" may include phenyl(lower)alkoxy [e.g., phenylmethoxy, (1- or 2-)-phenylethoxy, phenylpropoxy, 2-phenyl-1-methylpropoxy, 3-phenyl-2,2-dimethylpropoxy,  
30 (1- or 2- or 3- or 4-)phenylbutoxy, (1- or 2- or 3- or 4- or 5-)phenylpentyloxy, (1- or 2- or 3- or 4- or 5- or 6-phenylhexyloxy, etc.), naphthyl(lower)alkoxy [e.g. naphthylmethoxy, (1- or 2-)naphthylethoxy, 1-naphthylpropoxy, 2-naphthyl-1-methylpropoxy, 3-naphthyl-  
35 2,2-dimethylpropoxy, (1- or 2- or 3- or 4-)naphthylbutoxy,

31

03097 0519  
"E2260880"

(1- or 2- or 3- or 4- or 5-)naphthylpentyloxy, (1- or 2- or 3- or 4- or 5- or 6-)naphthylhexyloxy, etc.], and the like,

5 in which the preferred one may be naphthyl(C<sub>1</sub>-C<sub>4</sub>)alkoxy, and the more preferred one may be naphthylmethoxy.

Suitable example of "(lower)alkanoyl" moiety in the term of "ar(lower)alkoxy(lower)alkanoyl which may have one or more suitable substituent(s)" can be referred to aforementioned "lower alkanoyl",

10 in which the preferred one may be (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, and the more preferred one may be formyl.

Suitable example of "suitable substituent(s)" in the term of "ar(lower)alkoxy(lower)alkanoyl which may have one or more suitable substituent(s)" can be referred to aforementioned "suitable substituent(s)",

15 in which the preferred one may be lower alkoxy, higher alkoxy, lower alkyl and higher alkyl, and the more preferred one may be higher alkoxy, and the much more preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the most preferred one may be heptyloxy.

Suitable example of "arylamino" moiety in the term of "arylamino(lower)alkanoyl which may have one or more suitable substituent(s)" may include phenylamino, mesitylamino, tolylamino, naphthylamino, anthrylamino and the like,

25 in which the preferred one may be phenylamino and naphthylamino.

Suitable example of "lower alkanoyl" moiety in the term of "arylamino(lower)alkanoyl which may have one or more suitable substituent(s)" can be referred to aforementioned "lower alkanoyl",

30 in which the preferred one may be (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, and the more preferred one may be formyl.

35 Suitable example of "suitable substituent(s)" in the

32

08809723, 052197

term of "arylamino(lower)alkanoyl which may have one or more suitable substituent(s)" can be referred to aforementioned "suitable substituent(s)",

5 in which the preferred one may be lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, aryl which may have 1 to 3 lower alkoxy and aryl which may have 1 to 3 higher alkoxy, and the more preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and phenyl which may have 1 to 3 (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the most preferred one may be heptyloxy and phenyl which may  
10 have heptyloxy.

Suitable example of "lower alkanoyl" in the term of "lower alkanoyl substituted with pyrazolyl which has lower alkyl and aryl having higher alkoxy" can be referred to aforementioned "lower alkanoyl", in which the preferred  
15 one may be (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, and the most preferred one may be formyl.

Suitable example of "lower alkyl" in the term of "lower alkanoyl substituted with pyrazolyl which has lower alkyl and aryl having higher alkoxy" can be referred to aforementioned "lower alkyl", in which the preferred one  
20 may be (C<sub>1</sub>-C<sub>4</sub>)alkyl, and the most preferred one may be methyl.

Suitable example of "aryl" in the term of "lower alkanoyl substituted with pyrazolyl which has lower alkyl and aryl having higher alkoxy" can be referred to aforementioned "aryl", in which the preferred one may be  
25 phenyl.

Suitable example of "higher alkoxy" in the term of "lower alkanoyl substituted with pyrazolyl which has lower alkyl and aryl having higher alkoxy" can be referred to aforementioned "higher alkoxy", in which the preferred one  
30 may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the most preferred one may be octyloxy.

35 Suitable example of "lower alkoxy(higher)alkanoyl" in

33

08809723-052197

the term of "lower alkoxy(higher)alkanoyl, in which higher alkanoyl may have one or more suitable substituent(s)" may be (C<sub>1</sub>-C<sub>4</sub>)alkoxy(C<sub>7</sub>-C<sub>20</sub>)alkanoyl, in which the preferred one may be methoxyoctadecanoyl.

5        Suitable example of "suitable substituent(s)" in the term of "lower alkoxy(higher)alkanoyl, in which higher alkanoyl may have one or more suitable substituent(s)" may be amino and aforementioned "protected amino", in which the preferred one may be amino and  
10        ar(lower)alkoxycarbonylamino, and the most preferred one may be amino and benzyloxycarbonylamino.

15        Suitable example of "aroyl" in the term of "aroyl substituted with aryl having heterocycloxy, in which heterocycloxy may have one or more suitable substituent(s)" can be referred to aforementioned "aroyl", in which the preferred one may be benzoyl.

20        Suitable example of "aryl" in the term of "aroyl substituted with aryl having heterocycloxy, in which heterocycloxy may have one or more suitable substituent(s)" can be referred to aforementioned "aryl", in which the preferred one may be phenyl.

25        Suitable example of "heterocyclic" moiety in the term of "aroyl substituted with aryl having heterocycloxy, in which heterocycloxy may have one or more suitable substituent(s)" can be referred to aforementioned "heterocyclic" moiety, in which the preferred one may be unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s), and the most preferred  
30        one may be pyridazinyl.

35        Suitable example of "suitable substituent(s)" in the term of "aroyl substituted with aryl having heterocycloxy, in which heterocycloxy may have one or more suitable substituent(s)" may be aryl, in which the preferred one may be phenyl.

Suitable example of "aroyl" in the term of "aroyl substituted with cyclo(lower)alkyl having lower alkyl" can be referred to aforementioned "aroyl", in which the preferred one may be benzoyl.

5        Suitable example of "cyclo(lower)alkyl" in the term of "aroyl substituted with cyclo(lower)alkyl having lower alkyl" can be referred to aforementioned "cyclo(lower)alkyl", in which the preferred one may be cyclohexyl.

10       Suitable example of "lower alkyl" in the term of "aroyl substituted with cyclo(lower)alkyl having lower alkyl" can be referred to aforementioned "lower alkyl", in which the preferred one may be pentyl.

15       Suitable example of "higher alkyl" in the term of "indolylcarbonyl having higher alkyl" can be referred to aforementioned "higher alkyl", in which the preferred one may be decyl.

20       Suitable example of "lower alkyl" in the term of "naphthoyl having lower alkyl" can be referred to aforementioned "lower alkyl", in which the preferred one may be hexyl.

25       Suitable example of "higher alkyl" in the term of "naphthoyl having higher alkyl" can be referred to aforementioned "higher alkyl", in which the preferred one may be heptyl.

30       Suitable example of "lower alkoxy(higher)alkoxy" in the term of "naphthoyl having lower alkoxy(higher)alkoxy" may be (C<sub>1</sub>-C<sub>4</sub>)alkoxy(C<sub>7</sub>-C<sub>14</sub>)alkoxy, in which the preferred one may be methoxyoctyloxy.

35       Suitable example of "aroyl" in the term of "aroyl

08809723 052197

35

substituted with aryl having lower  
alkoxy(lower)alkoxy(higher)alkoxy", "aroyle substituted  
with aryl having lower alkoxy(lower)alkoxy", "aroyle  
substituted with aryl which has aryl having lower alkoxy",  
5 "aroyle substituted with aryl which has aryl having lower  
alkoxy(lower)alkoxy", "aroyle substituted with aryl having  
heterocyclicoxy(higher)alkoxy", "aroyle substituted with  
aryl having aryloxy(lower)alkoxy" and "aroyle substituted  
with aryl having heterocycliccarbonyl(higher)alkoxy" can  
10 be referred to aforementioned "aroyle", in which the  
preferred one may be benzoyl.

Suitable example of "aryl" in abovementioned terms  
can be referred to aforementioned "aryl", in which the  
preferred one may be phenyl.

15 Suitable example of "lower alkoxy(lower)alkoxy-  
(higher)alkoxy" in the term of "aroyle substituted with  
aryl having lower alkoxy(lower)alkoxy(higher)alkoxy" may  
be (C<sub>1</sub>-C<sub>4</sub>)alkoxy(C<sub>1</sub>-C<sub>4</sub>)alkoxy(C<sub>7</sub>-C<sub>14</sub>)alkoxy, in which the  
20 preferred one may be ethoxyethoxyoctyloxy.

Suitable example of "lower alkoxy(lower)alkoxy" in  
the term of "aroyle substituted with aryl having lower  
alkoxy(lower)alkoxy" may be (C<sub>1</sub>-C<sub>4</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)alkoxy, in  
25 which the preferred one may be propoxyhexyloxy.

Suitable example of "lower alkoxy" in the term of  
"aroyle substituted with aryl which has phenyl having lower  
alkoxy" may be (C<sub>3</sub>-C<sub>6</sub>)alkoxy, in which the preferred one  
30 may be butoxy.

Suitable example of "lower alkoxy(lower)alkoxy" in  
the term of "aroyle substituted with aryl which has phenyl  
having lower alkoxy(lower)alkoxy" may be (C<sub>1</sub>-C<sub>4</sub>)alkoxy-  
35 (C<sub>3</sub>-C<sub>6</sub>)alkoxy, in which the preferred one may be

36

08009723.052197

methoxypentyloxy and methoxyhexyloxy.

Suitable example of "heterocyclic" moiety in the term of "aroyl substituted with aryl having heterocyclicoxy(higher)alkoxy" can be referred to aforementioned "heterocyclic" moiety, in which the preferred one may be saturated 3 to 8-membered heteromonocyclic group containing an oxygen atom, and the most preferred one may be tetrahydropyranyl.

Suitable example of "higher alkoxy" moiety in the term of "aroyl substituted with aryl having heterocyclicoxy(higher)alkoxy" may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, in which the preferred one may be octyloxy.

Suitable example of "aryloxy(lower)alkoxy" in the term of "aroyl substituted with aryl having aryloxy(lower)alkoxy" may be phenoxy(C<sub>3</sub>-C<sub>6</sub>)alkoxy, in which the preferred one may be phoxypentyloxy.

Suitable example of "heterocyclic" moiety in the term of "aroyl substituted with aryl having heterocycliccarbonyl(higher)alkoxy" can be referred to aforementioned "heterocyclic" moiety, in which the preferred one may be saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s), and the most preferred one may be piperidyl.

Suitable example of "higher alkoxy" moiety in the term of "aroyl substituted with aryl having heterocycliccarbonyl(higher)alkoxy" can be referred to aforementioned "higher alkoxy", in which the preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the most preferred one may be heptyloxy.

Suitable example of "lower alkanoyl" in the term of "lower alkanoyl substituted with oxazolyl which has aryl

00009723.052197

37



having higher alkoxy" can be referred to aforementioned "lower alkanoyl", in which the preferred one may be (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, and the most preferred one may be formyl.

5      Suitable example of "aryl" in the term of "lower alkanoyl substituted with oxazolyl which has aryl having higher alkoxy" can be referred to aforementioned "aryl", in which the preferred one may be phenyl.

10      Suitable example of "higher alkoxy" in the term of "lower alkanoyl substituted with oxazolyl which has aryl having higher alkoxy" can be referred to aforementioned "higher alkoxy", in which the preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the most preferred one may be octyloxy.

15      Suitable example of "lower alkanoyl" in the term of "lower alkanoyl substituted with furyl which has aryl substituted with aryl having lower alkoxy" can be referred to aforementioned "lower alkanoyl", in which the preferred one may be (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, and the most preferred one may be formyl.

20      Suitable example of "aryl" in the term of "lower alkanoyl substituted with furyl which has aryl substituted with aryl having lower alkoxy" can be referred to aforementioned "aryl", in which the preferred one may be phenyl.

25      Suitable example of "lower alkoxy" in the term of "lower alkanoyl substituted with furyl which has aryl substituted with aryl having lower alkoxy" can be referred to aforementioned "lower alkoxy", in which the preferred one may be (C<sub>1</sub>-C<sub>4</sub>)alkoxy, and the most preferred one may be butoxy.

30      Suitable example of "lower alkanoyl" in the term of "lower alkanoyl substituted with triazolyl which has oxo and aryl having higher alkyl" can be referred to

34

08809723.052197

aforementioned "lower alkanoyl", in which the preferred one may be (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, and the most preferred one may be formyl.

5        Suitable example of "higher alkyl" in the term of "lower alkanoyl substituted with triazolyl which has oxo and aryl having higher alkyl" can be referred to aforementioned "higher alkyl", in which the preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkyl, and the most preferred one may be octyl.

10       Suitable example of "aryl" in the term of "lower alkanoyl substituted with triazolyl which has oxo and aryl having higher alkyl" can be referred to aforementioned "aryl", in which the preferred one may be phenyl.

15       Suitable example of "higher alkanoyl" in the term of "higher alkanoyl having hydroxy" can be referred to aforementioned "higher alkanoyl", in which the preferred one may be (C<sub>7</sub>-C<sub>20</sub>)alkanoyl, and the most preferred one may be hexadecanoyl.

20       Suitable example of "higher alkanoyl" in the term of "higher alkanoyl having ar(lower)alkyl and hydroxy" can be referred to aforementioned "higher alkanoyl", in which the preferred one may be (C<sub>7</sub>-C<sub>20</sub>)alkanoyl, and the most preferred one may be hexadecanoyl.

25       Suitable example of "ar(lower)alkyl" in the term of "higher alkanoyl having ar(lower)alkyl and hydroxy" can be referred to aforementioned "ar(lower)alkyl", in which the preferred one may be phenyl(C<sub>1</sub>-C<sub>4</sub>)alkyl, and the most preferred one may be benzyl.

30       Suitable example of "(C<sub>2</sub>-C<sub>6</sub>)alkanoyl" in the terms of "(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl having higher alkoxy, in which (C<sub>2</sub>-C<sub>6</sub>)alkanoyl may have amino or protected amino" may include acetyl, propanoyl, butanoyl,

35

39

08809723 052197  
261250 22/60880

pentanoyl, hexanoyl, and the like, in which the preferred one may be acetyl and propanoyl.

Suitable example of "aryl" in the term of "(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl having higher alkoxy, in which (C<sub>2</sub>-C<sub>6</sub>)alkanoyl may have amino or protected amino" can be referred to aforementioned "aryl", in which the preferred one may be phenyl.

Suitable example of "higher alkoxy" in the term of "(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl having higher alkoxy, in which (C<sub>2</sub>-C<sub>6</sub>)alkanoyl may have amino or protected amino" can be referred to aforementioned "higher alkoxy", in which the preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the most preferred one may be octyloxy.

Suitable example of "protected amino" in the term of "(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl having higher alkoxy, in which (C<sub>2</sub>-C<sub>6</sub>)alkanoyl may have amino or protected amino" can be referred to aforementioned "protected amino", in which the preferred one may be ar(lower)alkoxycarbonylamino, and the most preferred one may be benzyloxycarbonylamino.

The process for preparing the object polypeptide compound [I] or a salt thereof of the present invention are explained in detail in the following.

#### Process 1

The object polypeptide compound [I] or a salt thereof can be prepared by reacting the compound [II] or its reactive derivative at the amino group or a salt thereof with the compound [III] or its reactive derivative at the carboxy group or a salt thereof.

Suitable reactive derivative at the carboxy group of the compound [III] may include an acid halide, an acid anhydride, an activated amide, an activated ester, and the like. Suitable examples of the reactive derivatives may

40

be an acid chloride; an acid azide; a mixed acid anhydride with an acid such as substituted phosphoric acid [e.g., dialkylphosphoric acid, phenylphosphoric acid, diphenylphosphoric acid, dibenzylphosphoric acid, halogenated phosphoric acid, etc.], dialkylphosphorous acid, sulfurous acid, thiosulfuric acid, sulfuric acid, sulfonic acid [e.g., methanesulfonic acid, etc.], aliphatic carboxylic acid [e.g., acetic acid, propionic acid, butyric acid, isobutyric acid, pivalic acid, pentanoic acid, isopentanoic acid, 2-ethylbutyric acid, trichloroacetic acid, etc.]; or aromatic carboxylic acid [e.g., benzoic acid, etc.]; a symmetrical acid anhydride; an activated amide with imidazole, 4-substituted imidazole, dimethylpyrazole, triazole, tetrazole or 1-hydroxy-1H-benzotriazole; or an activated ester [e.g., cyanomethyl ester, methoxymethyl ester, dimethyliminomethyl  $[(CH_3)_2N^+=CH-]$  ester, vinyl ester, propargyl ester, p-nitrophenyl ester, 2,4-dinitrophenyl ester, trichlorophenyl ester, pentachlorophenyl ester, mesylphenyl ester, phenylazophenyl ester, phenyl thioester, p-nitrophenyl thioester, p-cresyl thioester, carboxymethyl thioester, pyranyl ester, pyridyl ester, piperidyl ester, 8-quinolyl thioester, etc.], or an ester with a N-hydroxy compound [e.g. N,N-dimethylhydroxylamine, 1-hydroxy-2-(1H)-pyridone, N-hydroxysuccinimide, N-hydroxyphthalimide, 1-hydroxy-1H-benzotriazole, etc.], and the like. These reactive derivatives can optionally be selected from them according to the mind of the compound [III] to be used.

Suitable salts of the compound [III] and its reactive derivative can be referred to the ones as exemplified for the object polypeptide compound [I].

The reaction is usually carried out in a conventional solvent such as water, alcohol [e.g., methanol, ethanol,

41

etc.], acetone, dioxane, acetonitrile, chloroform, methylene chloride, ethylene chloride, tetrahydrofuran, ethyl acetate, N,N-dimethylformamide, pyridine or any other organic solvent which does not adversely influence the reaction. These conventional solvent may also be used in a mixture with water.

In this reaction, when the compound [III] is used in a free acid form or its salt form, the reaction is preferably carried out in the presence of a conventional condensing agent such as N,N'-dicyclohexylcarbodiimide; N-cyclohexyl-N'-morpholinoethylcarbodiimide; N-cyclohexyl-N'-(4-diethylaminocyclohexyl)carbodiimide; N,N'-diethylcarbodiimide, N,N'-diisopropylcarbodiimide; N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide, N,N-carbonylbis-(2-methylimidazole); pentamethyleneketene-N-cyclohexylimine; diphenylketene-N-cyclohexylimine; ethoxyacetylene; 1-alkoxy-2-chloroethylene; trialkyl phosphite; ethyl polyphosphate; isopropyl polyphosphate; phosphorus oxychloride (phosphoryl chloride); phosphorus trichloride; thionyl chloride; oxalyl chloride; lower alkyl haloformate [e.g., ethyl chloroformate, isopropyl chloroformate, etc.]; triphenylphosphine; 2-ethyl-7-hydroxybenzisoxazolium salt; 2-ethyl-5-(m-sulfophenyl)isoxazolium hydroxide intramolecular salt; 1-(p-chlorobenzenesulfonyloxy)-6-chloro-1H-benzotriazole; so-called Vilsmeier reagent prepared by the reaction of N,N-dimethylformamide with thionyl chloride, phosgene, trichloromethyl chloroformate, phosphorous oxychloride, methanesulfonyl chloride, etc.; or the like.

The reaction may also be carried out in the presence of an inorganic or organic base such as an alkali metal carbonate, alkali metal bicarbonate, tri(lower)alkylamine, pyridine, di(lower)alkylaminopyridine (e.g.,

4-dimethylaminopyridine, etc.), N-(lower)alkylmorpholine, N,N-di(lower)alkylbenzylamine, or the like.

The reaction temperature is not critical, and the reaction is usually carried out under cooling to warming.

5

The starting compound [II] is a known compound. It can be prepared by fermentation and synthetic processes disclosed in EP 0462531 A2.

10 A culture of Coleophoma sp. F-11899, which is used in said fermentation process, has been deposited with National Institute of Bioscience and Human-Technology Agency of Industrial Science and Technology (former name: Fermentation Research Institute Agency of Industrial Science and Technology) (1-3, Higashi 1-chome, Tsukuba-shi, IBARAKI 305, JAPAN) on October 26, 1989 under the  
15 number of FERM BP-2635.

20 The compounds obtained by the above Process 1 can be isolated and purified by a conventional method such as pulverization, recrystallization, column-chromatography, high-performance liquid chromatography (HPLC), reprecipitation, or the like.

25 The compounds obtained by the above Process 1 may be obtained as its hydrate, and its hydrate is included within the scope of this invention.

30 It is to be noted that each of the object compound (I) may include one or more stereoisomer such as optical isomer(s) and geometrical isomer(s) due to asymmetric carbon atom(s) and double bond(s) and all such isomers and mixture thereof are included within the scope of this invention.

35

43

08809723.052197

Biological property of the polypeptide  
compound [I] of the present invention

5 In order to show the usefulness of the polypeptide  
compound [I] of the present invention, the biological data  
of the representative compound is explained in the  
following.

Test 1 (Antimicrobial activity) :

10 In vitro antimicrobial activity of the compound of  
Example 17 disclosed later was determined by the two-fold  
agar-plate dilution method as described below.

Test Method

15 One loopful of an overnight culture of each test  
microorganism in Sabouraud broth containing 2% Glucose  
( $10^5$  viable cells per ml) was streaked on yeast nitrogen  
base dextrose agar (YNBDA) containing graded  
concentrations of the object polypeptide compound [I], and  
20 the minimal inhibitory concentration (MIC) was expressed  
in terms of  $\mu\text{g/ml}$  after incubation at  $30^\circ\text{C}$  for 24 hours.

Test Result

MIC ( $\mu\text{g/ml}$ )

25

Test compound Test organism	The compound of <u>Example 17</u>
T <sub>10440</sub> candida albicans FP-633	0.2

30 From the test result, it is realized that the object  
polypeptide compound [I] of the present invention has an  
antimicrobial activity (especially, antifungal activity).

35 The pharmaceutical composition of the present

44

invention can be used in the form of a pharmaceutical preparation, for example, in solid, semisolid or liquid form, which contains the object polypeptide compound (I) or a pharmaceutically acceptable salt thereof, as an  
5 active ingredient in admixture with an organic or inorganic carrier or excipient which is suitable for rectal; pulmonary (nasal or buccal inhalation); ocular; external (topical); oral administration; parenteral (including subcutaneous, intravenous and intramuscular)  
10 administrations; insufflation (including aerosols from metered dose inhalator); nebulizer; or dry powder inhalator.

The active ingredient may be compounded, for example,  
15 with the usual non-toxic, pharmaceutically acceptable carriers in a solid form such as granules, tablets, dragees, pellets, troches, capsules, or suppositories; creams, ointments; aerosols; powders for insufflation; in a liquid form such as solutions, emulsions, or  
20 suspensions for injection; ingestion; eye drops; and any other form suitable for use. And, if necessary, there may be included in the above preparation auxiliary substance such as stabilizing, thickening, wetting, emulsifying and coloring agents; perfumes or buffer; or any other commonly  
25 may be used as additives.

The object polypeptide compound [I] or a pharmaceutically acceptable salt thereof is/are included in the pharmaceutical composition in an amount sufficient to produce the desired antimicrobial effect upon the  
30 process or condition of diseases.

For applying the composition to human, it is preferable to apply it by intravenous, intramuscular, pulmonary, oral administration, or insufflation. While the dosage of therapeutically effective amount of the  
35 object polypeptide compound [I] varies from and also



depends upon the age and condition of each individual patient to be treated, in the case of intravenous administration, a daily dose of 0.01-20 mg of the object polypeptide compound [I] per kg weight of human being in the case of intramuscular administration, a daily dose of 0.1-20 mg of the object polypeptide compound [I] per kg weight of human being, in case of oral administration, a daily dose of 0.5-50 mg of the object polypeptide compound [I] per kg weight of human being is generally given for treating or preventing infectious diseases.

Especially in case of the treatment of prevention of Pneumocystis carinii infection, the followings are to be noted.

For administration by inhalation, the compounds of the present invention are conveniently delivered in the form of an aerosol spray presentation from pressurized as powders which may be formulated and the powder compositions may be inhaled with the aid of an insufflation powder inhaler device. The preferred delivery system for inhalation is a metered dose inhalation aerosol, which may be formulated as a suspension or solution of compound in suitable propellants such as fluorocarbons or hydrocarbons.

Because of desirability to directly treat lung and bronchi, aerosol administration is a preferred method of administration. Insufflation is also a desirable method, especially where infection may have spread to ears and other body cavities.

Alternatively, parenteral administration may be employed using drip intravenous administration.

The following Preparations and Examples are given for the purpose of illustrating the present invention in more detail.

Preparation 1

To a suspension of 1-(4-Hydroxyphenyl)-4-tert-butoxycarbonylpiperazine (3 g) and potassium carbonate (0.82 g) in N,N-dimethylformamide (15 ml) was added octyl bromide (1.87 ml). The mixture was stirred for 10 hours at 70°C. The reaction mixture was added to a mixture of water and ethyl acetate. The organic layer was taken, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel, and eluted with (hexane : ethyl acetate = 9:1). The fractions containing the object compound were combined, and evaporated under reduced pressure to give 1-(4-n-Octyloxyphenyl)-4-tert-butoxycarbonylpiperazine (2.71 g).

IR (KBr) : 1687, 1513, 1241  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.2\text{Hz}$ ), 1.2-1.4 (10H, m), 1.48 (9H, s), 1.65-1.85 (2H, m), 3.00 (4H, t,  $J=5.2\text{Hz}$ ), 3.57 (4H, t,  $J=5.2\text{Hz}$ ), 3.90 (2H, t,  $J=6.5\text{Hz}$ ), 6.83 (2H, dd,  $J=6.4$  and 2.1Hz), 6.89 (2H, dd,  $J=6.4$  and 2.1Hz)

Preparation 2

A solution of 1-(4-n-Octyloxyphenyl)-4-tert-butoxycarbonylpiperazine (2.61 g) in trifluoroacetic acid (20 ml) was stirred for 4 hours at ambient temperature. The reaction mixture was evaporated under reduced pressure, and to the residue was added a mixture of 1N NaOH aqueous solution and ethyl acetate. The organic layer was taken, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give 1-(4-n-Octyloxyphenyl)piperazine (0.86 g).

IR (KBr) : 2923, 1513, 1259, 831  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.4\text{Hz}$ ), 1.2-1.53

47

(10H, m), 1.65-1.85 (2H, m), 3.03 (4H, s), 3.90  
(2H, t, J=6.5Hz), 6.83 (2H, dd, J=6.4 and  
2.9Hz), 6.90 (2H, dd, J=6.4 and 2.9Hz)

APCI-MASS : m/z = 291 ( $M^+ + 1$ )

5

### Preparation 3

To a suspension of 1-(4-n-Octyloxyphenyl)piperazine  
(1 g) and potassium carbonate (0.476 g) in N,N-dimethyl-  
formamide (1 ml) was added p-fluorobenzonitrile (0.347 g),  
10 and stirred for 5 hours at 160°C. The reaction mixture  
was added to a mixture of water and ethyl acetate. The  
organic layer was taken, and dried over magnesium sulfate.  
The magnesium sulfate was filtered off, and the filtrate  
was evaporated under reduced pressure to give 4-[4-(4-n-  
15 Octyloxyphenyl)piperazin-1-yl]benzonitrile (0.93 g).

IR (KBr) : 2848, 2217, 1604, 1511, 1241  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t, J=6.8Hz), 1.2-1.53

(10H, m), 1.65-1.85 (2H, m), 3.20 (4H, t,  
J=5.4Hz), 3.48 (4H, t, J=5.4Hz), 3.91 (2H, t,  
20 J=6.5Hz), 6.8-7.0 (6H, m), 7.52 (2H, d, J=8.9Hz)

APCI-MASS : m/z = 392 ( $M^+ + 1$ )

### Preparation 4

A mixture of 2,4-Dihydroxybenzaldehyde (5.52 g),  
25 potassium carbonate (6.08 g) and octyl bromide (7.73 g) in  
acetonitrile (55 ml) was stirred for 16 hours at 60°C.  
The solvent of reaction mixture was removed under reduced  
pressure, and the residue was dissolved in ethyl acetate,  
and washed with water and brine. The separated organic  
30 layer was dried over magnesium sulfate. The magnesium  
sulfate was filtered off, and the filtrate was evaporated  
under reduced pressure. The residue was subjected to  
column chromatography on silica gel and eluted with  
(hexane : ethyl acetate = 9:1) to give 2-Hydroxy-4-  
35 octyloxybenzaldehyde (6.73 g).

48

08809723-052197  
26 FEB 90 12:50

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.89 (3H, t, J=8.8Hz), 1.2-1.5  
(10H, m), 1.8-2.0 (2H, m), 4.0-4.2 (2H, m), 6.42  
(1H, s), 6.52 (1H, d, J=8.7Hz), 7.79 (1H, d,  
J=8.7Hz), 10.33 (1H, s)

5 APCI-MASS : m/z = 257 (M<sup>+</sup>+1)

The following compound was obtained according to a  
similar manner to that of Preparation 4.

10 Preparation 5

Methyl 3,4-dipentyloxybenzoate

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.93 (6H, t, J=6.0 and 9.0Hz), 1.3-  
2.0 (12H, m), 3.88 (3H, s), 4.04 (4H, m),  
6.86 (1H, d, J=8.4Hz), 7.53 (1H, d, J=2.0Hz),  
15 7.63 (1H, dd, J=8.4 and 2.0Hz)

APCI-MASS : m/z = 309 (M<sup>+</sup>+1)

Preparation 6

A mixture of 4-bromo-4'-pentylbiphenyl (5.04 g),  
20 trimethylsilylacetylene (2.4 ml),  
tetrakis(triphenylphosphine)palladium (0.96 g),  
triphenylphosphine (0.22 g) and cuprous iodide (95 mg) in  
piperidine (10 ml) was heated for an hour under  
atmospheric pressure of nitrogen at 90°C. The reaction  
25 mixture was poured into a mixture of cold water and ethyl  
acetate, and adjusted to about pH 1 with 6N hydrochloric  
acid. The separated organic layer was washed with water  
and brine, and dried over magnesium sulfate. The  
magnesium sulfate was filtered off, and the filtrate was  
30 evaporated under reduced pressure to give crude 2-[4-(4-  
pentylphenyl)phenyl]-1-trimethylsilylacetylene, which was  
used for the next reaction without further purification.  
Crude mixture was dissolved in a mixture of  
dichloromethane (10 ml) and methanol (10 ml), and to the  
35 solution was added potassium carbonate (2.75 g) at 0°C.

The mixture was allowed to warm to ambient temperature, and stirred for another 2 hours. The reaction mixture was poured into a mixture of cold water and ethyl acetate, and the resultant precipitate was filtered off. The filtrate was adjusted to about pH 7 with 1N hydrochloric acid, and washed with brine, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give a crude powder, which was subjected to column chromatography on silica gel (300 ml), and eluted with a mixture of (n-hexane : ethyl acetate = 99:1 - 97:3, V/V) to give 4-(4-Pentylphenyl)phenylacetylene (2.09g).

IR (Nujol) : 3274, 1490  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.4\text{Hz}$ ), 1.30-1.50 (4H, m), 1.50-1.80 (2H, m), 2.64 (2H, t,  $J=7.6\text{Hz}$ ), 7.20-7.30 (2H, m), 7.45-7.60 (6H, m)

APCI-MASS :  $m/z = 281$  ( $M^++1$  + MeOH)

The following compound was obtained according to a similar manner to that of Preparation 6.

#### Preparation 7

6-Heptyloxynaphthalen-2-yl-acetylene

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.5\text{Hz}$ ), 1.20-1.60 (8H, m), 1.70-1.90 (2H, m), 3.10 (1H, s), 4.07 (2H, t,  $J=6.5\text{Hz}$ ), 7.08 (1H, d,  $J=2.5\text{Hz}$ ), 7.15 (1H, dd,  $J=2.5$  and  $8.9\text{Hz}$ ), 7.47 (1H, dd,  $J=1.6$  and  $8.5\text{Hz}$ ), 7.64 (1H, d,  $J=7.3\text{Hz}$ ), 7.68 (1H, d,  $J=8.5\text{Hz}$ ), 7.94 (1H, d,  $J=1.6\text{Hz}$ )

APCI-MASS :  $m/z = 267$  ( $M^++1$ )

#### Preparation 8

To a solution of 4-(4-Pentylphenyl)phenylacetylene (2.09 g) in tetrahydrofuran (30 ml) was added dropwise a solution of lithium diisobutylamide in a mixture of

267250 22/60880  
tetrahydrofuran and n-hexane (1.60 M, 5.6 ml) at -75°C, and the resultant mixture was stirred for an hour at -78°C. To the mixture was added methyl chloroformate (0.72 ml), and the reaction mixture was allowed to warm to ambient temperature. The solution was diluted with ethyl acetate, and washed in turn with water and brine, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give a crude product, which was subjected to column chromatography on silica gel (150 ml), and eluted with a mixture of (n-hexane : ethyl acetate = 100:0 - 9:1, V/V) to give Methyl 3-[4-(4-pentylphenyl)phenyl]propionate (2.20 g).

IR (Nujol) : 2225, 1712  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.5\text{Hz}$ ), 1.25-1.50 (4H, m), 1.52-1.80 (2H, m), 2.64 (2H, t,  $J=7.6\text{Hz}$ ), 3.85 (3H, s), 7.20-7.35 (2H, m), 7.40-7.70 (6H, m)

APCI-MASS :  $m/z = 307$  ( $M^++1$ )

The following compound was obtained according to a similar manner to that of Preparation 8.

#### Preparation 9

Methyl 3-(6-heptyloxynaphthalen-2-yl)propionate

IR (Nujol) : 2219, 1704, 1621  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.5\text{Hz}$ ), 1.20-1.60 (8H, m), 1.70-2.00 (2H, m), 3.86 (3H, s), 4.08 (2H, t,  $J=6.5\text{Hz}$ ), 7.10 (1H, d,  $J=2.5\text{Hz}$ ), 7.17 (1H, dd,  $J=2.5$  and  $8.9\text{Hz}$ ), 7.52 (1H, dd,  $J=1.6$  and  $8.5\text{Hz}$ ), 7.68 (1H, d,  $J=7.3\text{Hz}$ ), 7.72 (1H, d,  $J=8.5\text{Hz}$ ), 8.06 (1H, d,  $J=1.6\text{Hz}$ )

APCI-MASS :  $m/z = 325$  ( $M^++1$ )

#### Preparation 10

A mixture of 4-bromo-4'-pentylbiphenyl (5.0 g), methyl acrylate (2.2 ml), palladium acetate (0.11 g) and tris(o-tolyl)phosphine (0.60 g) in triethylamine (16 ml) was refluxed for 15 hours under nitrogen atmosphere. The reaction mixture was poured into a mixture of cold water and ethyl acetate, and adjusted to about pH 1.5 with 6N hydrochloric acid. The separated organic layer was washed in turn with water and brine, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give a crude powder, which was subjected to column chromatography on silica gel (200 ml), and eluted with a mixture of (n-hexane : ethyl acetate = 100:0 - 94:6, V/V) to give Methyl 3-[4-(4-pentylphenyl)phenyl]acrylate (4.48 g).

IR (Nujol) : 1718, 1637  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.91 (3H, t,  $J=6.7\text{Hz}$ ), 1.20-1.50 (4H, m), 1.50-1.80 (2H, m), 2.65 (2H, t,  $J=7.4\text{Hz}$ ), 3.82 (3H, s), 6.47 (1H, d,  $J=16.0\text{Hz}$ ), 7.20-7.35 (2H, m), 7.45-7.68 (6H, m), 7.73 (1H, d,  $J=16.0\text{Hz}$ )

APCI-MASS :  $m/z = 309 (M^++1)$

The following compounds (Preparations 11 to 13) were obtained according to a similar manner to that of Preparation 10.

#### Preparation 11

Methyl 3-(6-heptyloxynaphthalen-2-yl)acrylate

IR (Nujol) : 1716, 1625, 1459  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.5\text{Hz}$ ), 1.20-1.65 (8H, m), 1.76-1.93 (2H, m), 3.82 (3H, s), 4.07 (2H, t,  $J=6.5\text{Hz}$ ), 6.49 (1H, d,  $J=16.0\text{Hz}$ ), 7.05-7.20 (2H, m), 7.55-7.90 (5H, m)

APCI-MS :  $m/z = 327 (M^++1)$

Preparation 12

Methyl 3-[4-(4-heptylphenyl)phenyl]acrylate

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.88 (3H, t, J=6.5Hz), 1.15-1.50  
(8H, m), 1.50-1.75 (2H, m), 2.64 (2H, t,  
J=7.6Hz), 3.81 (3H, s), 6.46 (1H, d, J=16.0Hz),  
7.26 (2H, d, J=8.2Hz), 7.52 (2H, d, J=8.2Hz),  
7.59 (6H, s), 7.73 (1H, d, J=16.0Hz)

APCI-MASS : m/z = 337 (M<sup>+</sup>+1)

Preparation 13

Methyl 3-[4-(4-pentyloxyphenyl)phenyl]acrylate

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.94 (3H, t, J=7.0Hz), 1.30-1.60  
(4H, m), 1.70-1.93 (2H, m), 3.82 (3H, s), 4.00  
(2H, t, J=6.7Hz), 6.45 (1H, d, J=16.0Hz), 6.90-  
7.05 (2H, m), 7.48-8.65 (6H, m), 7.72 (1H, d,  
J=16.0Hz)

APCI-MASS : m/z = 325 (M<sup>+</sup>+1)

Preparation 14

A mixture of 6-Heptyloxynaphthalen-2-carboxylic acid  
(1.00 g) and thionyl chloride (5 ml) was stirred for 18  
hours at ambient temperature, and concentrated under  
reduced pressure to give crude 6-heptyloxy-2-naphthoyl  
chloride. To a mixture of ethyl isonipecotinate (605 mg),  
triethylamine (425 mg) and N,N-dimethylaminopyridine (10  
mg) in dichloromethane (10 ml) was added crude 6-  
heptyloxy-2-naphthoyl chloride, and the mixture was  
stirred for 2 hours at ambient temperature, and diluted  
with dichloromethane. The mixture was washed with water,  
1N hydrochloric acid and brine, and dried over magnesium  
sulfate. The magnesium sulfate was filtered off, and  
filtrate was evaporated under reduced pressure. The  
residue was subjected to column chromatography on silica  
gel, and eluted with (n-hexane : ethyl acetate = 3:1) to  
give 4-Ethoxycarbonyl-1-(6-heptyloxy-2-



naphthoyl)piperidine (1.20 g).

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.6\text{Hz}$ ), 1.2-2.0  
(19H, m), 2.5-2.7 (1H, m), 3.0-3.2 (2H, m), 4.1-  
4.3 (4H, m), 7.1-7.2 (2H, m), 7.44 (1H, dd,  
5  $J=8.4$  and  $1.7\text{Hz}$ ), 7.72 (1H, d,  $J=3.9\text{Hz}$ ), 7.77  
(1H, d,  $J=3.9\text{Hz}$ ), 7.82 (1H, s)

APCI-MASS :  $m/z = 426 (M^++1)$

Preparation 15

10 To a mixture of Methyl 3,4-diaminobenzoate (1.91 g)  
and triethylamine (0.56 g) in N,N-dimethylformamide (20  
ml) was added decanoyl chloride (2.31 g), and the mixture  
was stirred for an hour at  $0^\circ\text{C}$ . The reaction mixture was  
15 diluted with ethyl acetate, and washed with water and  
brine. The separated organic layer was dried over  
magnesium sulfate. The magnesium sulfate was filtered  
off, and filtrate was evaporated under reduced pressure.  
The residue was dissolved in methanol (20 ml), and conc.  
20 sulfuric acid (0.05 ml) was added, and the mixture was  
stirred for 6 hours at  $60^\circ\text{C}$ . After cooling, the reaction  
mixture was evaporated under reduced pressure. The  
residue was diluted with ethyl acetate, and washed with  
water and brine. The separated organic layer was dried  
25 over magnesium sulfate. The magnesium sulfate was  
filtered off, and filtrate was evaporated under reduced  
pressure. Purification of the residue by column  
chromatography on silica gel eluted with (n-hexane : ethyl  
acetate = 3:1) gave

5-Methoxycarbonyl-2-nonylbenzimidazole (1.40 g).

30 IR (KBr pelet) : 2923, 1718, 1623, 1544, 1438, 1413,  
1288, 1213, 1085,  $750\text{ cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.84 (3H, t,  $J=6.7\text{Hz}$ ), 1.1-1.4  
(12H, m), 1.7-1.9 (2H, m), 2.83 (2H, t,  
 $J=7.4\text{Hz}$ ), 7.56 (1H, d,  $J=8.4\text{Hz}$ ), 7.78 (1H, d,  
35  $J=8.4\text{Hz}$ ), 8.07 (1H, s)

54

0809723-052197

APCI-MASS :  $m/z = 303 (M^+ + 1)$

Preparation 16

To a mixture of dimethylmalonate (4 ml), 2-hydroxy-4-octyloxybenzaldehyde (2.50 g) and piperidine (0.1 ml) in methanol (10 ml) was added acetic acid (0.01 ml), and the mixture was stirred for 3 hours at 70°C. The solvents were removed under reduced pressure, and the residue was dissolved in ethyl acetate, and washed with 0.5N hydrochloric acid, water and brine, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and filtrate was evaporated under reduced pressure, and the precipitate was collected by filtration, and washed with n-hexane, and dried to give Methyl 7-octyloxycoumarin-3-carboxylate (0.94 g).

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, m), 1.2-1.6 (10H, m), 1.7-1.8 (2H, m), 3.81 (3H, s), 4.11 (2H, t,  $J=6.4\text{Hz}$ ), 6.9-7.1 (2H, m), 7.83 (1H, d,  $J=9.0\text{Hz}$ ), 8.75 (1H, s)

APCI-MASS :  $m/z = 333 (M^+ + 1)$

Preparation 17

To a mixture of sodium hydride (423 mg) and 4-octylphenol (2.06 g) in tetrahydrofuran (16 ml) was added dropwise ethyl 2-chloroacetoacetate at ambient temperature. The mixture was stirred for 6 hours at 70°C under nitrogen atmosphere, and poured into saturated ammonium chloride aqueous solution. The solution was extracted with ethyl acetate, and the organic layer was washed with water and brine, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure. The residue was added to conc.  $\text{H}_2\text{SO}_4$  (10 ml) at 0°C, and mixture was stirred for 10 minutes. The reaction mixture was poured into ice-water, and adjusted to pH 7.0 with 1N

NaOH aqueous solution, and extracted with ethyl acetate. The organic layer was washed with water and brine, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure. The residue was subjected to column-chromatography on silica gel, and eluted with (hexane : ethyl acetate = 95:5). The fractions containing the object compound were combined, and evaporated under reduced pressure to give Ethyl 3-methyl 5-octylbenzo[b]furan-2-carboxylate (1.44 g).

IR (Neat) : 2925, 2854, 1712, 1596, 1463, 1292, 1149, 1089  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.7\text{Hz}$ ), 1.2-1.5 (10H, m), 1.44 (3H, t,  $J=7.1\text{Hz}$ ), 1.6-1.8 (2H, m), 2.58 (3H, s), 2.71 (2H, t,  $J=8.0\text{Hz}$ ), 4.45 (2H, t,  $J=7.1\text{Hz}$ ), 7.2-7.5 (3H, m)

APCI-MASS :  $m/z = 317$  ( $M^+ + 1$ )

#### Preparation 18

To a solution of Ethyl 3-amino-4-hydroxybenzoate (1.81 g) and triethylamine (1.53 ml) in dichloromethane (20 ml) was dropwise added decanoyl chloride (2.01 ml) at  $0^\circ\text{C}$ . The reaction mixture was stirred for 48 hours at ambient temperature, and washed with water, 0.5N hydrochloric acid, water and brine. The separated organic layer was dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure. To the residue dissolved in xylene (30 ml) was added p-toluene sulfonic acid monohydrate (0.5 g), and the mixture was stirred for 4 hours at  $130^\circ\text{C}$ . Ethyl acetate was added to the mixture, and washed with water and brine. The separated organic layer was dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure. Purification of the residue by

column chromatography on silica gel elluted with  
(n-hexane : ethyl acetate = 9:1, V/V) gave Ethyl 2-nonyl  
benzo[b]oxazole-6-carboxylate (2.36 g).

5 IR (KBr pelet) : 2914, 1722, 1621, 1575, 1470,  
1429, 1365, 1290, 1203, 1151, 1115, 1081,  
1022  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.7\text{Hz}$ ), 1.2-1.4 (12H,  
m), 1.42 (3H, t,  $J=7.2\text{Hz}$ ), 1.90 (2H, m), 2.95  
10 (2H, t,  $J=7.4\text{Hz}$ ), 4.40 (2H, q,  $J=7.0\text{Hz}$ ), 7.50  
(1H, d,  $J=8.5\text{Hz}$ ), 8.06 (1H, d,  $J=8.5\text{Hz}$ ), 8.37  
(1H, s)

APCI-MASS :  $m/z = 318$  ( $M^++1$ )

#### Preparation 19

15 A mixture of Methyl 3,4-diaminobenzoate (1.84 g) and  
4-hexyloxy benzaldehyde (2.30 g) in nitrobenzene (40 ml)  
was stirred for 48 hours at  $145^\circ\text{C}$ . After cooling, the  
mixture was evaporated under reduced pressure.  
Purification of the residue by column chromatography on  
20 silica gel eluted with (n-hexane : ethyl acetate = 2:1)  
gave 5-Methoxycarbonyl-2-(4-hexyloxyphenyl)benzimidazole  
(1.19 g).

25 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.4\text{Hz}$ ), 1.2-1.9 (8H,  
m), 3.92 (3H, s), 3.90-4.1 (2H, m), 6.93 (2H, d,  
 $J=8.9\text{Hz}$ ), 7.5-7.8 (1H, br), 7.94 (1H, dd,  $J=8.5$   
and  $1.5\text{Hz}$ ), 8.03 (1H, d,  $J=8.9\text{Hz}$ ), 8.2-8.4 (1H,  
br)

APCI-MASS :  $m/z = 353$  ( $M^++1$ )

#### 30 Preparation 20

A mixture of Methyl 3-[4-(4-pentylphenyl)phenyl]-  
acrylate (2.0 g) and 10% palladium on carbon (50% wet, 0.2  
g) in tetrahydrofuran (20 ml) was stirred for 8 hours  
under atmospheric pressure of hydrogen at ambient  
35 temperature. The catalyst was filtered off, and the

filtrate was evaporated under reduced pressure to give Methyl 3-[4-(4-pentylphenyl)phenyl]propionate (1.93 g).

5 NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.90 (3H, t, J=6.8Hz), 1.25-1.50 (4H, m), 1.50-1.75 (2H, m), 2.55-2.75 (4H, m), 2.99 (2H, t, J=8.0Hz), 3.68 (3H, s), 7.10-7.30 (4H, m), 7.40-7.60 (4H, m)

APCI-MASS : m/z = 311 (M<sup>+</sup>+1)

#### Preparation 21

10 A mixture of Methyl 3-[4-(4-pentyloxyphenyl)phenyl]-acrylate (2.70 g) and platinum oxide (0.41 g) in tetrahydrofuran (40 ml) was stirred for 8 hours under 3 atom of hydrogen at ambient temperature. The catalyst was filtered off, and the filtrate was evaporated under  
15 reduced pressure to give Methyl 3-[4-(4-pentyloxyphenyl)phenyl]propionate (2.70 g).

20 NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.94 (3H, t, J=7.0Hz), 1.28-1.60 (4H, m), 1.60-1.95 (2H, m), 2.55-2.78 (2H, m), 2.98 (2H, t, J=7.8Hz), 3.98 (2H, t, J=6.5Hz), 6.85-7.05 (2H, m), 7.05-7.30 (2H, m), 7.40-7.55 (4H, m)

APCI-MASS : m/z = 327 (M<sup>+</sup>+1)

25 The following compound was obtained according to a similar manner to that of Preparation 21.

#### Preparation 22

Methyl 3-(6-heptyloxynaphthalen-2-yl)propionate

30 NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.90 (3H, t, J=6.5Hz), 1.20-1.70 (8H, m), 1.70-1.93 (2H, m), 2.70 (2H, t, J=7.7Hz), 3.07 (2H, t, J=7.7Hz), 3.67 (3H, s), 4.05 (2H, t, J=6.5Hz), 7.02-7.20 (2H, m), 7.20-7.38 (2H, m), 7.55 (1H, s), 7.66 (1H, dd, J=3.0 and 8.5Hz)

35 APCI-MASS : m/z = 329 (M<sup>+</sup>+1)

Preparation 23

To a mixture of Methyl 3-[4-(4-pentylphenyl)phenyl]-acrylate (0.41 g) in tetrahydrofuran (5 ml) was added 3N NaOH aqueous solution (1.3 ml), and the resultant mixture was heated to 85°C for 10 hours. The reaction mixture was poured into a mixture of cold water and ethyl acetate, and adjusted to about pH 2 with 6N hydrochloric acid. The separated organic layer was washed in turn with water and brine, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give 3-[4-(4-Pentylphenyl)phenyl]acrylic acid (0.41 g).

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.87 (3H, t, J=7.5Hz), 1.15-1.46 (4H, m), 1.48-1.70 (2H, m), 2.61 (2H, t, J=7.4Hz), 6.56 (1H, d, J=16.0Hz), 7.29 (2H, d, J=8.2Hz), 7.60 (2H, d, J=4.0Hz), 7.66 (2H, d, J=4.0Hz), 7.68-7.85 (3H, m)

APCI-MASS : m/z = 295 (M<sup>+</sup>+1)

The following compounds (Preparations 24 to 31) were obtained according to a similar manner to that of Preparation 23.

Preparation 24

3-[4-(4-Pentyloxyphenyl)phenyl]propionic acid

IR (Nujol) : 1697, 1606, 1500 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.94 (3H, t, J=7.1Hz), 1.25-1.60 (4H, m), 1.70-1.95 (2H, m), 2.72 (2H, t, J=7.5Hz), 3.00 (2H, t, J=7.5Hz), 3.99 (2H, t, J=6.5Hz), 6.95 (2H, dd, J=2.1 and 6.7Hz), 7.25 (2H, d, J=8.2Hz), 7.40-7.60 (4H, m)

APCI-MASS : m/z = 313 (M<sup>+</sup>+1)

Preparation 25

3-[4-(4-Heptylphenyl)phenyl]propionic acid

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.88 (3H, t, J=6.8Hz), 1.15-1.50  
(8H, m), 1.50-1.78 (2H, m), 2.65 (2H, t,  
J=7.6Hz), 6.48 (1H, d, J=16.0Hz), 7.27 (2H, d,  
J=8.2Hz), 7.53 (2H, d, J=8.2Hz), 7.63 (4H, m),  
7.83 (1H, d, J=16.0Hz)

APCI-MASS : m/z = 323 (M<sup>+</sup>+1)

Preparation 26

3-[4-(4-Pentylphenyl)phenyl]propionic acid

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.90 (3H, t, J=6.4Hz), 1.20-1.50  
(4H, m), 1.50-1.75 (2H, m), 2.64 (2H, t,  
J=8.0Hz), 2.67 (2H, t, J=9.6Hz), 3.00 (2H, t,  
J=8.0Hz), 7.15-7.38 (4H, m), 7.38-7.60 (4H, m)

APCI-MASS : m/z = 297 (M<sup>+</sup>+1)

Preparation 27

3-(6-Heptyloxynaphthalen-2-yl)propionic acid

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.90 (3H, t, J=6.5Hz), 1.20-1.65  
(8H, m), 1.75-2.00 (2H, m), 2.75 (2H, t,  
J=7.7Hz), 3.09 (2H, t, J=7.7Hz), 4.06 (2H, t,  
J=6.5Hz), 7.05-7.15 (2H, m), 7.15-7.35 (2H, m),  
7.50-7.73 (2H, m)

APCI-MASS : m/z = 315 (M<sup>+</sup>+1)

Preparation 28

3-(6-Heptyloxynaphthalen-2-yl)acrylic acid

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.90 (3H, t, J=6.5Hz), 1.15-1.60  
(8H, m), 1.75-1.95 (2H, m), 4.09 (2H, t,  
J=6.5Hz), 6.51 (1H, d, J=16.0Hz), 7.09-7.30 (2H,  
m), 7.65-8.00 (5H, m)

Preparation 29

3-[4-(4-Pentylphenyl)phenyl]propionic acid

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.91 (3H, t, J=6.5Hz), 1.23-1.50  
(4H, m), 1.50-1.80 (2H, m), 2.65 (2H, t,

J=7.6Hz), 7.27 (2H, d, J=8.2Hz), 7.51 (2H, d, J=8.2Hz), 7.58-7.80 (4H, m)

APCI-MASS :  $m/z = 325 (M^+ + 1 + \text{MeOH})$

5 Preparation 30

3-(6-Heptyloxynaphthalen-2-yl)propionic acid

IR (Nujol) : 2645, 2198, 1670, 1627  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.85 (3H, t, J=6.5Hz), 1.10-1.60 (8H, m), 1.65-1.90 (2H, m), 4.10 (2H, t,

10 J=6.5Hz), 7.24 (1H, dd, J=2.4 and 8.9Hz), 7.39 (1H, d, J=2.5Hz), 7.55 (1H, dd, J=1.6 and 8.5Hz), 7.8-8.0 (2H, m), 8.22 (1H, d, J=1.6Hz)

APCI-MASS :  $m/z = 343 (M^+ + 1 + \text{MeOH})$

15 Preparation 31

4-[5-(4-Pentyloxyphenyl)isoxazolyl-3-yl]benzoic acid

IR (KBr) : 2939, 2867, 1681, 1614, 1429, 1255, 1178, 821  $\text{cm}^{-1}$

20 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.91 (3H, t, J=7.1Hz), 1.3-1.5 (4H, m), 1.6-1.8 (2H, m), 4.04 (2H, t, J=6.5Hz), 7.11 (2H, d, J=8.9Hz), 7.54 (1H, s), 7.85 (2H, d, J=8.9Hz), 7.98 (2H, d, J=8.6Hz), 8.11 (2H, d, J=8.6Hz)

APCI-MASS :  $m/z = 352 (M+H)^+$

25

Preparation 32

To a solution of Ethyl 3-methyl-5-octylbenzo[b]furan-2-carboxylate (1.44 g) in ethanol (20 ml) was added 10% NaOH aqueous solution (2.2 ml), and stirred for 2 hours at ambient temperature, and evaporated under reduced pressure. The residue was adjusted to pH 3.0 with 1N hydrochloric acid, and extracted with ethyl acetate. The organic layer was washed with brine, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to

35



give 3-Methyl-5-octylbenzo[b]furan-2-carboxylic acid (1.00 g).

IR (KBr pelet) : 2923, 1689, 1664, 1581, 1456, 1319, 1159, 933  $\text{cm}^{-1}$

5 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.7\text{Hz}$ ),  
1.2-1.5 (10H, m), 1.5-1.8 (2H, m), 2.49 (3H, s),  
2.69 (2H, t,  $J=7.9\text{Hz}$ ), 7.32 (1H, dd,  $J=8.5$  and  
1.7Hz), 7.52 (1H, d,  $J=8.5\text{Hz}$ ), 7.54 (1H, d,  
 $J=1.7\text{Hz}$ ), 13.2-13.5 (1H, br)

10 APCI-MASS :  $m/z = 289$  ( $M^++1$ )

The following compounds (Preparations 33 to 39) were obtained according to a similar manner to that of Preparation 32.

15

Preparation 33

3,4-Dipentyloxybenzoic acid

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.89 (6H, t,  $J=6.8\text{Hz}$ ),  
1.2-1.5 (8H, m), 1.6-1.8 (4H, m), 3.9-4.1 (4H,  
20 m), 7.02 (1H, d,  $J=8.4\text{Hz}$ ), 7.43 (1H, d,  
 $J=1.7\text{Hz}$ ), 7.53 (1H, dd,  $J=8.4$  and  $1.7\text{Hz}$ )

APCI-MASS :  $m/z = 295$  ( $M^++1$ )

Preparation 34

25 1-(6-Heptyloxy-2-naphthoyl)piperidine-4-carboxylic  
acid

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.7\text{Hz}$ ), 1.2-2.0  
(14H, m), 2.5-2.6 (1H, m), 2.9-3.2 (2H, br),  
3.25 (2H, s), 4.09 (2H, t,  $J=6.5\text{Hz}$ ), 7.20 (1H,  
30 dd,  $J=8.9$  and  $2.4\text{Hz}$ ), 7.36 (1H, d,  $J=2.3\text{Hz}$ ),  
7.43 (1H, dd,  $J=8.4$  and  $1.5\text{Hz}$ ), 7.8-8.0 (3H, m),  
12.30 (1H, br)

APCI-MASS :  $m/z = 398$  ( $M^++1$ )

35

62

Preparation 35

7-Octyloxycoumarin-3-carboxylic acid

IR (KBr) : 1748, 1625, 1558, 1467, 1430, 1386, 1360,  
1257, 1217, 1120  $\text{cm}^{-1}$

5 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.8\text{Hz}$ ), 1.2-1.5  
(10H, m), 1.6-1.8 (2H, m), 4.11 (2H, t,  
 $J=6.4\text{Hz}$ ), 6.9-7.1 (2H, m), 7.82 (1H, d,  
 $J=8.9\text{Hz}$ ), 8.72 (1H, s), 12.98 (1H, br)

APCI-MASS :  $m/z = 319$  ( $M^++1$ )

10

Preparation 36

4-(4-Pentyloxyphenyl)cinnamic acid

IR (Nujol) : 2923, 1675, 1500, 1290, 1223, 985,  
821  $\text{cm}^{-1}$

15 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.90 (3H, t,  $J=7.0\text{Hz}$ ), 1.3-1.5  
(4H, m), 1.6-1.8 (2H, m), 4.01 (2H, t,  $J=6.5\text{Hz}$ ),  
6.54 (1H, d,  $J=16.0\text{Hz}$ ), 7.02 (2H, d,  $J=8.8\text{Hz}$ ),  
7.5-7.8 (7H, m)

APCI-MASS :  $m/z = 311$  ( $M^++1$ )

20

Preparation 37

2-Nonylbenzoxazole-6-carboxylic acid

25 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.84 (3H, t,  $J=6.7\text{Hz}$ ), 1.2-1.5  
(12H, m), 1.7-1.9 (2H, m), 2.96 (2H, t,  
 $J=7.4\text{Hz}$ ), 7.76 (1H, d,  $J=8.4\text{Hz}$ ), 7.98 (1H, d,  
 $J=8.4\text{Hz}$ ), 8.19 (1H, s)

APCI-MASS :  $m/z = 290$  ( $M^++1$ )

Preparation 38

30 2-(4-Hexyloxyphenyl)benzimidazole-5-carboxylic acid

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.8-1.0 (3H, m), 1.3-1.6 (6H, m),  
1.7-1.8 (2H, m), 4.06 (2H, t,  $J=6.4\text{Hz}$ ), 7.12  
(2H, d,  $J=8.8\text{Hz}$ ), 7.6-7.9 (2H, m), 8.1-8.2 (3H,  
m), 13.00 (1H, br)

35

APCI-MASS :  $m/z = 339$  ( $M^++1$ )

63

08809723.052197

Preparation 39

2-Nonylbenzimidazole-5-carboxylic acid

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.85 (3H, t, J=6.7Hz), 1.1-1.4  
(12H, m), 2.7-2.9 (2H, m), 2.96 (2H, t,  
J=7.6Hz), 3.6-5.2 (1H, br), 7.66 (1H, d,  
J=8.4Hz), 7.90 (1H, d, J=8.4Hz), 8.15 (1H, s)

APCI-MASS : m/z = 289 (M<sup>+</sup>+1)

Preparation 40

A solution of 4-[4-(4-Octyloxyphenyl)piperazin-1-yl]benzonitrile (0.5 g) in 20% H<sub>2</sub>SO<sub>4</sub> aqueous solution (30 ml) and acetic acid (20 ml) was refluxed for 9 hours. The reaction mixture was pulverized with water. The precipitate was collected by filtration, and added to a mixture of water, tetrahydrofuran and ethyl acetate, and adjusted to pH 2.5 with 1N NaOH aqueous solution. The organic layer was taken, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give 4-[4-(4-Octyloxyphenyl)piperazin-1-yl]benzoic acid (388 mg).

IR (KBr) : 2929, 1664, 1600, 1510, 1240 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.86 (3H, t, J=6.6Hz), 1.2-1.5  
(10H, m), 1.5-1.8 (2H, m), 3.13 (4H, t,  
J=5.3Hz), 3.44 (4H, t, J=5.3Hz), 3.88 (2H, t,  
J=6.5Hz), 6.83 (2H, d, J=9.2Hz), 6.94 (2H, d,  
J=9.2Hz), 7.02 (2H, d, J=9.0Hz), 7.79 (2H, d,  
J=9.0Hz)

APCI-MASS : m/z = 411 (M<sup>+</sup>+1)

Preparation 41

To a suspension of sodium hydride (60% suspension in mineral oil) (0.296 g) in N,N-dimethylformamide (14 ml) was added 1,2,4-triazole (0.511 g) and 4-[4-(8-bromooctyloxy)phenyl]benzoic acid (1 g), and was stirred for 5 hours at 120°C. The reaction mixture was added to a

64

5 mixture of water and ethyl acetate, and adjusted to pH 2.5 with conc. hydrochloric acid. The organic layer was taken and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give 4-[4-[8-(1,2,4-Triazol-1-yl)octyloxy]phenyl]benzoic acid (0.81 g).

IR (KBr) : 2940, 1689, 1604, 1297, 1189  $\text{cm}^{-1}$

10 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.1-1.53 (8H, m), 1.6-1.9 (4H, m), 4.00 (2H, t,  $J=6.3\text{Hz}$ ), 4.16 (2H, t,  $J=7.0\text{Hz}$ ), 7.03 (2H, d,  $J=8.7\text{Hz}$ ), 7.67 (2H, d,  $J=8.7\text{Hz}$ ), 7.75 (2H, d,  $J=8.4\text{Hz}$ ), 7.95 (1H, s), 7.99 (2H, d,  $J=8.4\text{Hz}$ ), 8.51 (1H, s), 12.9 (1H, s)

15 APCI-MASS :  $m/z = 394 (M^+ + 1)$

#### Preparation 42

20 A mixture of 2-Carbamoyl-5-methoxybenzo[b]thiophene (2.0 g), acetic acid (5 ml) and 48% hydrobromic acid (20 ml) was stirred for 16 hours at  $110^\circ\text{C}$ , and the mixture was poured into the ice-water. The resulting precipitate was collected by filtration, and dried to give 5-Hydroxybenzo[b]thiophene-2-carboxylic acid (1.66 g).

25 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 7.03 (1H, dd,  $J=8.8$  and  $0.6\text{Hz}$ ), 7.31 (1H, d,  $J=0.6\text{Hz}$ ), 7.81 (1H, d,  $J=8.8\text{Hz}$ ), 7.96 (1H, s), 9.64 (1H, s), 13.32 (1H, s)

APCI-MASS :  $m/z = 195 (M^+ + 1)$

#### Preparation 43

30 A solution of (S)-2-Tert-butoxycarbonyl-1,2,3,4-tetrahydro-7-hydroxyisoquinoline-3-carboxylic acid (1 g) in a mixture of 10% NaOH aqueous solution (2.73 ml) and dimethylsulfoxide (11 ml) was stirred for half an hour at  $80^\circ\text{C}$ . Then, octyl bromide (0.589 ml) was added thereto, and stirred for 4 hours at  $60^\circ\text{C}$ . The reaction mixture was added to a mixture of water and ethyl acetate, and

35

65

08809723.052197

adjusted to pH 2.5 with conc. hydrochloric acid. The organic layer was taken, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give (S)-2-Tert-butoxycarbonyl-1,2,3,4-tetrahydro-7-octyloxyisoquinoline-3-carboxylic acid (1.30 g).

IR (Neat) : 2929, 1743, 1704, 1164  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.1\text{Hz}$ ), 1.1-1.6 (10H, m), 1.41 + 1.51 (9H, s, cis + trans), 1.75 (2H, quint,  $J=6.5\text{Hz}$ ), 3.10 (2H, m), 3.90 (2H, t,  $J=3.9\text{Hz}$ ), 4.42 (1H, d,  $J=16.8\text{Hz}$ ), 4.65 (1H, d,  $J=16.8\text{Hz}$ ), 4.74 + 5.09 (1H, m, cis + trans), 6.5-6.8 (2H, m), 7.03 (1H, d,  $J=8.3\text{Hz}$ )

APCI-MASS :  $m/z = 306$  ( $M^+ + 1$ -Boc)

The following compounds (Preparations 44 to 45) were obtained according to a similar manner to that of Preparation 43.

Preparation 44

5-Octyloxybenzo[b]thiophene-2-carboxylic acid

IR (KBr) : 1673, 1666, 1600, 1517, 1409, 1267, 1214, 1153, 865  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.7\text{Hz}$ ), 1.2-1.5 (10H, m), 1.7-1.9 (2H, m), 4.02 (2H, t,  $J=6.4\text{Hz}$ ), 7.13 (1H, dd,  $J=8.9$  and  $0.6\text{Hz}$ ), 7.51 (1H, d,  $J=0.6\text{Hz}$ ), 7.90 (1H, d,  $J=9.0\text{Hz}$ ), 7.99 (1H, s)

APCI-MASS :  $m/z = 307$  ( $M^+ + 1$ )

Preparation 45

4-[4-(4-Hexyloxyphenyl)piperazin-1-yl]benzoic acid dihydrochloride

IR (KBr) : 1668, 1600, 1510, 1228  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.9\text{Hz}$ ), 1.2-1.5

66

(6H, m), 1.6-1.9 (2H, m), 3.0-3.2 (4H, m), 3.3-3.5 (4H, m), 3.88 (2H, t, J=6.3Hz), 6.83 (2H, d, J=9Hz), 6.9-7.1 (4H, m), 7.79 (2H, d, J=8.8Hz), 12.32 (1H, s)

5 APCI-MASS : m/z = 383 (M+H<sup>+</sup>)

#### Preparation 46

To a suspension of dimethyl terephthalate (1.94 g) and potassium t-butoxide (2.24 g) in tetrahydrofuran (30 ml) was added 4-pentyloxyacetophenone (1.59 g) in tetrahydrofuran (10 ml) at 70°C dropwise. The mixture was refluxed for 30 minutes and poured into 1N HCl (50 ml). The mixture was extracted with ethyl acetate (100 ml) and the organic layer was washed with H<sub>2</sub>O (100 ml), brine (100 ml) and evaporated under reduced pressure. The residue was triturated with acetonitrile (20 ml), collected by filtration and dried under reduced pressure to give 1-(4-Methoxycarbonylphenyl)-3-(4-pentyloxyphenyl)propane-1,3-dione (2.41 g) as yellow solid.

20 IR (KBr) : 3475, 2956, 2923, 1720, 1606, 1508, 1284, 1176, 1108, 769 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 0.95 (3H, t, J=7.0Hz), 1.3-1.5 (4H, m), 1.7-2.0 (2H, m), 3.96 (3H, s), 4.04 (2H, t, J=6.5Hz), 6.82 (1H, s), 6.96 (2H, d, J=8.9Hz), 8.0-8.1 (4H, m), 8.14 (2H, m, J=8.7Hz), 12-13 (1H, br)

25 APCI-MASS : m/z = 369 (M+H<sup>+</sup>)

#### Preparation 47

30 The solution of 1-(4-Methoxycarbonylphenyl)-3-(4-pentyloxyphenyl)propane-1,3-dione (1.00 g) and hydroxylamine hydrochloride (567 mg) in methanol (10 ml) was refluxed for 10 hours. The reaction mixture was diluted with ethyl acetate (50 ml) and washed with water (50 ml x 2), brine (50 ml). The organic layer was dried

67

over magnesium sulfate and the solvents were removed under reduced pressure. The residue was triturated with acetonitrile (10 ml), collected by filtration, and dried under reduced pressure to give Methyl 4-[5-(4-pentyloxyphenyl)isoxazol-3-yl]benzoate (0.74 g).

IR (KBr) : 2942, 2873, 1716, 1616, 1508, 1280, 1108  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.95 (3H, t,  $J=6.9\text{Hz}$ ), 1.3-1.6 (4H, m), 1.8-2.0 (2H, m), 3.95 (3H, s), 4.02 (2H, t,  $J=6.5\text{Hz}$ ), 6.74 (1H, s), 6.99 (2H, d,  $J=8.8\text{Hz}$ ), 7.76 (2H, d,  $J=8.8\text{Hz}$ ), 7.93 (2H, d,  $J=8.5\text{Hz}$ ), 8.14 (2H, d,  $J=8.5\text{Hz}$ )

APCI-MASS :  $m/z = 366 (M+H)^+$

#### Preparation 48

A solution of 4-[4-(8-Bromooctyloxy)phenyl]benzoic acid (1 g) in a mixture of sodium methylate (28% solution in methanol) (10 ml) and N,N-dimethylformamide (5 ml) was refluxed for 5 hours. The reaction mixture was added to a mixture of water and ethyl acetate and adjusted to pH 2.0 with conc. HCl. The organic layer was taken and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give 4-[4-(8-Methoxyoctyloxy)phenyl]benzoic acid (0.77 g).

IR (KBr) : 2935, 1685, 835, 773  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.27-1.7 (10H, m), 1.7-1.95 (2H, m), 3.34 (3H, s), 3.38 (2H, t,  $J=6.4\text{Hz}$ ), 4.01 (2H, t,  $J=6.5\text{Hz}$ ), 6.99 (2H, d,  $J=8.7\text{Hz}$ ), 7.58 (2H, d,  $J=8.7\text{Hz}$ ), 7.66 (2H, d,  $J=8.4\text{Hz}$ ), 8.15 (2H, d,  $J=8.4\text{Hz}$ )

APCI-MASS :  $m/z = 339 (M^+ + H - H_2O)$

#### Preparation 49

To a suspension of 1-Hydroxybenzotriazole (0.283 g)

68

and 6-octyloxymethylpicolinic acid (0.505 g) in dichloromethane (15 ml) was added 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride (WSCD·HCl) (0.473 g), and stirred for 3 hours at ambient temperature. The reaction mixture was poured into water. The organic layer was taken, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give 1-(6-Octyloxymethylpicolinoyl)benzotriazole 3-oxide (737 mg).

IR (Neat) : 1793, 1654, 1591, 1039  $\text{cm}^{-1}$

The following compounds [Preparations 50 to 66] were obtained according to a similar manner to that of Preparation 49.

Preparation 50

1-[4-(4-Octyloxyphenyl)piperazin-1-yl]benzoyl]-benzotriazole 3-oxide

IR (KBr) : 1783, 1600, 1511, 1232, 1184  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.6\text{Hz}$ ), 1.2-1.65 (10H, m), 1.65-1.9 (2H, m), 3.24 (4H, t,  $J=5.3\text{Hz}$ ), 3.62 (4H, t,  $J=5.3\text{Hz}$ ), 3.93 (2H, t,  $J=6.5\text{Hz}$ ), 6.8-7.1 (6H, m), 7.35-7.63 (3H, m), 8.0-8.25 (3H, m)

Preparation 51

1-[4-[4-[8-(1,2,4-Triazol-1-yl)octyloxy]phenyl]-benzoyl]benzotriazole 3-oxide

IR (KBr) : 1776, 1600, 1193, 983  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.2-2.0 (12H, m), 4.03 (2H, t,  $J=6.4\text{Hz}$ ), 4.18 (2H, t,  $J=7.1\text{Hz}$ ), 7.02 (2H, d,  $J=8.7\text{Hz}$ ), 7.4-7.63 (3H, m), 7.63 (2H, d,  $J=8.7\text{Hz}$ ), 7.79 (2H, d,  $J=8.3\text{Hz}$ ), 7.95 (1H, s), 8.06 (1H, s), 8.12 (1H, d,  $J=7.7\text{Hz}$ ), 8.32 (2H, d,  $J=8.3\text{Hz}$ )

69



APCI-MASS :  $m/z = 511 (M^+ + 1)$

Preparation 52

1-[2-Methyl-2-(4-octyloxyphenoxy)propionyl]-  
5 benzotriazole 3-oxide

IR (Neat) : 2927, 1810, 1504, 1047  $\text{cm}^{-1}$

Preparation 53

1-[2-(4-Octyloxyphenoxy)propionyl]benzotriazole  
10 3-oxide

IR (KBr) : 2954, 1812, 1513, 1232  $\text{cm}^{-1}$

Preparation 54

1-[(S)-2-tert-Butoxycarbonyl-1,2,3,4-tetrahydro-7-  
15 octyloxyisoquinolin-3-yl-carbonyl]benzotriazole 3-oxide

IR (Neat) : 2929, 1816, 1739, 1704, 1392  $\text{cm}^{-1}$

Preparation 55

Succinimido 4-(4-n-octyloxyphenyl)piperazine-1-  
20 carboxylate

IR (KBr) : 2925, 1758, 1743, 1513, 1241  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.8\text{Hz}$ ), 1.2-1.5

(10H, m), 1.65-1.85 (2H, m), 2.83 (4H, s),

3.0-3.2 (2H, m), 3.6-3.85 (2H, m), 3.91 (2H, t,

25  $J=6.5\text{Hz}$ ), 6.84 (2H, dd,  $J=8.5$  and  $2.7\text{Hz}$ ), 6.90

(2H, dd,  $J=8.5$  and  $2.7\text{Hz}$ )

APCI-MASS :  $m/z = 432 (M^+ + 1)$

Preparation 56

(6-Heptyloxy-2-naphthyl)methylsuccinimido carbonate

IR (KBr) : 1878, 1832, 1787, 1735, 1209  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.2\text{Hz}$ ), 1.2-1.6 (8H,  
m), 1.73-2.0 (2H, m), 2.83 (4H, s), 4.07 (2H, t,

$J=6.5\text{Hz}$ ), 5.44 (2H, s), 7.13 (1H, d,  $J=2.4\text{Hz}$ ),

35 7.17 (1H, dd,  $J=8.8$  and  $2.4\text{Hz}$ ), 7.44 (1H, dd,

J=8.4 and 1.6Hz), 7.67-7.85 (3H, m)

Preparation 57

1-(3,4-Dipentyloxybenzoyl)benzotriazole 3-oxide

5 IR (KBr) : 2952, 1774, 1594, 1515, 1430, 1272, 1147,  
1089  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.9-1.1 (6H, m), 1.3-1.6 (8H, m),  
1.8-2.1 (4H, m), 4.0-4.2 (4H, m), 6.99 (1H, d,  
J=8.5Hz), 7.4-7.6 (3H, m), 7.68 (1H, d,  
10 J=2.0Hz), 7.92 (1H, dd, J=8.5 and 2.0Hz), 8.10  
(1H, d, J=8.5Hz)

APCI-MASS :  $m/z$  = 412 ( $M^+ + 1$ )

Preparation 58

15 1-(7-Octyloxycoumarin-3-yl-carbonyl)benzotriazole  
3-oxide

IR (KBr) : 2925, 1754, 1716, 1610, 1548, 1282, 1199,  
1172, 1139, 1064, 781, 750  $\text{cm}^{-1}$

20 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.86 (3H, t, J=7.8Hz), 1.2-1.5  
(10H, m), 1.6-1.8 (2H, m), 4.11 (2H, t,  
J=6.5Hz), 6.9-7.1 (2H, m), 7.41 (1H, t,  
J=7.2Hz), 7.54 (1H, t, J=7.2Hz), 7.72 (1H, d,  
J=8.3Hz), 7.82 (1H, d, J=8.3Hz), 7.99 (1H, d,  
J=8.3Hz), 8.72 (1H, s)

25 APCI-MASS :  $m/z$  = 436 ( $M^+ + 1$ )

Preparation 59

1-[4-(4-Pentyloxyphenyl)cinnamoyl]benzotriazole 3-  
oxide

30 IR (Nujol) : 2854, 1778, 1708, 1620, 1597, 1494,  
1459, 1434, 1377, 1350, 1250, 1188, 1138, 1086,  
978  $\text{cm}^{-1}$

Preparation 60

35 1-(5-Octyloxybenzo[b]thiophen-2-yl-carbonyl)-

71

06809723.052197  
267250.6260880

benzotriazole 3-oxide

IR (KBr) : 2950, 1776, 1517, 1342, 1211, 1151  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.7\text{Hz}$ ), 1.2-1.5  
(10H, m), 1.7-1.9 (2H, m), 4.01 (2H, t,  
5  $J=6.4\text{Hz}$ ), 7.13 (1H, dd,  $J=8.8$  and  $2.4\text{Hz}$ ), 7.42  
(1H, d,  $J=7.1\text{Hz}$ ), 7.5-7.6 (3H, m), 7.72 (1H, d,  
 $J=8.4\text{Hz}$ ), 7.89 (1H, d,  $J=8.8\text{Hz}$ ), 7.9-8.1 (2H, m)

APCI-MASS :  $m/z = 424$  ( $M^++1$ )

10 Preparation 61

1-(3-Methyl-5-octylbenzo[b]furan-2-yl-carbonyl)-  
benzotriazole 3-oxide

IR (KBr) : 1776, 1575, 1469, 1363, 1324, 1276, 1114,  
1027  $\text{cm}^{-1}$

15 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.7\text{Hz}$ ), 1.2-1.5  
(10H, m), 2.6-2.8 (2H, m), 2.71 (3H, s), 2.76  
(2H, t,  $J=7.4\text{Hz}$ ), 7.4-7.6 (6H, m), 8.12 (1H, s)

APCI-MASS :  $m/z = 406$  ( $M^++1$ )

20 Preparation 62

1-(2-Nonylbenzoxazol-5-yl-carbonyl)benzotriazole  
3-oxide

IR (KBr) : 2980, 1783, 1623, 1573, 1276, 1151, 1091,  
989  $\text{cm}^{-1}$

25 NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.84 (3H, t,  $J=6.8\text{Hz}$ ), 1.1-1.4  
(12H, m), 1.81 (2H, t,  $J=7.2\text{Hz}$ ), 2.96 (3H, t,  
 $J=7.4\text{Hz}$ ), 7.41 (1H, t,  $J=7.0\text{Hz}$ ), 7.54 (1H, t,  
 $J=7.0\text{Hz}$ ), 7.74 (2H, t,  $J=7.0\text{Hz}$ ), 7.98 (2H, d,  
 $J=7.0\text{Hz}$ ), 8.19 (1H, s)

30 APCI-MASS :  $m/z = 407$  ( $M^++1$ )

Preparation 63

1-[2-(4-Hexyloxyphenyl)benzimidazol-5-yl-carbonyl]-  
benzotriazole 3-oxide

35 IR (KBr) : 3160, 2931, 2863, 1778, 1612, 1502, 1448,

72

08809723.052197  
26T250"E260880

1388, 1294, 1247, 1174, 1097, 1010, 732  $\text{cm}^{-1}$   
NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.7\text{Hz}$ ), 1.2-1.5  
(6H, m), 1.7-1.8 (2H, m), 4.08 (2H, t,  $J=6.4\text{Hz}$ ),  
7.16 (2H, d,  $J=8.7\text{Hz}$ ), 7.6-8.4 (9H, m), 8.3-8.6  
(1H, br)  
APCI-MASS :  $m/z = 456 (M^++1)$

Preparation 64

1-[4-[4-(8-Methoxyoctyloxy)phenyl]benzoyl]-  
benzotriazole-3-oxide

IR (KBr) : 2931, 1793, 1770, 1600  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.2-1.7 (10H, m), 1.7-1.93 (2H, m),  
3.34 (3H, s), 3.38 (2H, t,  $J=6.4\text{Hz}$ ), 4.03 (2H,  
t,  $J=6.5\text{Hz}$ ), 7.03 (2H, d,  $J=8.8\text{Hz}$ ), 7.4-7.7 (3H,  
m), 7.63 (2H, d,  $J=8.8\text{Hz}$ ), 7.79 (2H, d,  
 $J=8.6\text{Hz}$ ), 8.12 (1H, d,  $J=8.2\text{Hz}$ ), 8.32 (2H, d,  
 $J=8.6\text{Hz}$ )

Preparation 65

1-[4-[4-(4-Hexyloxyphenyl)piperazin-1-  
yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 1770, 1604, 1510, 1232, 1186  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.91 (3H, t,  $J=6.6\text{Hz}$ ), 1.2-1.6 (6H,  
m), 1.6-1.9 (2H, m), 3.1-3.3 (4H, m), 3.5-3.7  
(4H, m), 3.93 (2H, t,  $J=6.5\text{Hz}$ ), 6.87 (2H, d,  
 $J=9.2\text{Hz}$ ), 6.96 (2H, d,  $J=9.2\text{Hz}$ ), 7.00 (2H, d,  
 $J=9.0\text{Hz}$ ), 7.3-7.7 (3H, m), 8.10 (1H, d,  
 $J=8.2\text{Hz}$ ), 8.15 (2H, d,  $J=9.0\text{Hz}$ )

APCI-MASS :  $m/z = 500 (M+H^+)$

Preparation 66

1-[4-[5-(4-Pentyloxyphenyl)isoxazol-3-yl]benzoyl]-  
benzotriazole 3-oxide

IR (KBr) : 2950, 2837, 1774, 1616, 1508, 1452, 1251,  
1006  $\text{cm}^{-1}$

73

NMR (CDCl<sub>3</sub>, δ) : 0.95 (3H, t, J=7.1Hz), 1.3-1.5 (4H, m), 1.8-2.0 (2H, m), 4.04 (2H, t, J=6.5Hz), 6.81 (1H, s), 7.0-7.1 (3H, m), 7.4-7.6 (3H, m), 7.80 (2H, d, J=8.8Hz), 8.0-8.2 (3H, m), 8.40 (2H, d, J=8.4Hz)

APCI-MASS : m/z = 469 (M+H)<sup>+</sup>

#### Preparation 67

To a suspension of 1-hydroxybenzotriazole (0.20 g) and 4-(4-pentylphenyl)cinnamic acid (0.40 g) in dichloromethane (12.0 ml) was added 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride (0.33 g) (WSCD·HCl), and the mixture was stirred for 12 hours at ambient temperature. The reaction mixture was diluted with dichloromethane, and washed with brine, and dried over magnesium sulfate. After magnesium sulfate was filtered off, evaporation of the filtrate and trituration with acetonitrile gave 1-[4-(4-Pentylphenyl)cinnamoyl]benzotriazole 3-oxide (0.24 g).

NMR (CDCl<sub>3</sub>, δ) : 0.91 (3H, t, J=6.6Hz), 1.20-1.50 (4H, m), 1.50-1.75 (2H, m), 2.66 (2H, t, J=8.0Hz), 7.20-8.25 (11H, m), 8.55 (1H, d, J=8.4Hz)

APCI-MASS : m/z = 412 (M<sup>+</sup>+1)

The following compounds (Preparations 68 to 73) were obtained according to a similar manner to that of Preparation 67.

#### Preparation 68

1-[3-[4-(4-Pentyloxyphenyl)phenyl]-2-propanoyl]-benzotriazole 3-oxide

NMR (CDCl<sub>3</sub>, δ) : 0.90-1.05 (3H, m), 1.30-1.65 (4H, m), 1.70-1.95 (2H, m), 3.10-3.60 (4H, m), 3.90-4.10 (2H, m), 6.88-7.08 (2H, m),

7.20-8.50 (10H, m)

APCI-MASS :  $m/z = 430 (M^+ + 1)$

Preparation 69

5 1-[4-(4-Heptylphenyl)cinnamoyl]benzotriazole 3-oxide

NMR ( $CDCl_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.7\text{Hz}$ ), 1.20-1.50

(8H, m), 1.50-1.80 (2H, m), 2.66 (2H, t,

$J=7.6\text{Hz}$ ), 6.70-8.60 (12H, m)

APCI-MASS :  $m/z = 440 (M^+ + 1)$

10

Preparation 70

1-[3-[4-(4-Pentylphenyl)phenyl]-2-propanoyl]-  
benzotriazole 3-oxide

NMR ( $CDCl_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.8\text{Hz}$ ), 1.20-1.50

15 (4H, m), 1.50-1.76 (2H, m), 2.63 (2H, t,

$J=7.4\text{Hz}$ ), 3.21 (2H, t,  $J=7.3\text{Hz}$ ), 3.51 (2H, t,

$J=7.3\text{Hz}$ ), 7.20-7.45 (4H, m), 7.45-7.70 (5H, m),

7.78 (1H, dt,  $J=1.0$  and  $7.2\text{Hz}$ ), 8.00 (1H, d,

$J=8.2\text{Hz}$ ), 8.42 (1H, d,  $J=8.4\text{Hz}$ )

20 APCI-MASS :  $m/z = 414 (M^+ + 1)$

Preparation 71

1-[3-(6-Heptyloxynaphthalen-2-yl)propanoyl]-  
benzotriazole 3-oxide

25 NMR ( $CDCl_3$ ,  $\delta$ ) : 0.80-1.10 (3H, m), 1.20-1.70 (8H,

m), 1.70-2.00 (2H, m), 3.10-3.70 (4H, m), 4.00-

4.18 (2H, m), 6.80-8.50 (10H, m)

APCI-MASS :  $m/z = 432 (M^+ + 1)$

30 Preparation 72

1-[3-(6-Heptyloxynaphthalen-2-yl)propenoyl]-  
benzotriazole 3-oxide

NMR ( $CDCl_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.5\text{Hz}$ ), 1.20-1.65

(8H, m), 1.75-1.95 (2H, m), 4.10 (2H, d,

35  $J=6.5\text{Hz}$ ), 6.75-8.62 (8H, m)

75

08009723.052197  
261250"E2260880

APCI-MASS :  $m/z = 430 (M^+ + 1)$

Preparation 73

1-(4-Hexylphenylbenzoyl)benzotriazole 3-oxide

5 NMR ( $CDCl_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=4.4\text{Hz}$ ), 1.2-1.5 (6H, m), 1.6-1.8 (2H, m), 2.68 (2H, t,  $J=8.0\text{Hz}$ ), 7.32 (2H, d,  $J=8.2\text{Hz}$ ), 7.4-7.7 (5H, m), 7.81 (2H, d,  $J=6.6\text{Hz}$ ), 8.10 (2H, d,  $J=8.1\text{Hz}$ ), 8.32 (2H, d,  $J=7.6\text{Hz}$ )

10 APCI-MASS :  $m/z = 400 (M^+ + 1)$

Preparation 74

261250 6260880  
15 To a solution of 4-octyloxyphenol (1 g) in dimethylformamide (10 ml) and pyridine (0.364 ml) was added N,N'-disuccinimidylcarbonate (1.16 g). The mixture was stirred for 12 hours at ambient temperature. The reaction mixture was added to a mixture of water and ethyl acetate. The organic layer was taken, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the  
20 filtrate was evaporated under reduced pressure to give 4-Octyloxyphenylsuccinimidyl carbonate (0.59 g).

IR (KBr) : 2927, 1876, 1832, 1735  $\text{cm}^{-1}$

25 NMR ( $CDCl_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.3\text{Hz}$ ), 1.2-1.55 (10H, m), 1.67-1.87 (2H, m), 2.87 (4H, s), 3.94 (2H, t,  $J=6.5\text{Hz}$ ), 6.89 (2H, d,  $J=9.2\text{Hz}$ ), 7.17 (2H, d,  $J=9.2\text{Hz}$ )

APCI-MASS :  $m/z = 364 (M^+ + 1)$

30 The following compounds (Preparations 75 to 88) were obtained according to a similar manner to that of Preparation 1.

Preparation 75

Methyl 4-[4-(6-phenylpyridazin-3-yl-oxy)phenyl]benzoate

35 IR (KBr) : 1708, 1427, 1280, 1187, 1112  $\text{cm}^{-1}$

74

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 3.95 (3H, s), 7.2-7.7 (10H, m),  
7.92 (1H, d, J=9.2Hz), 8.0-8.2 (4H, m)  
APCI-MASS : m/z = 383 (M+H)<sup>+</sup>

5 Preparation 76

Methyl 4-[4-(5-bromopentyloxy)phenyl]benzoate

IR (KBr) : 2946, 2871, 1716, 1602, 1294, 1199, 1112,  
837 cm<sup>-1</sup>

10 NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.7-2.0 (6H, m), 3.45 (2H, t,  
J=6.7Hz), 3.93 (3H, s), 4.02 (2H, t, J=6.1Hz), 6.97  
(2H, d, J=8.7Hz), 7.56 (2H, d, J=8.7Hz), 7.61 (2H,  
d, J=8.3Hz), 8.07 (2H, d, J=8.3Hz)  
APCI-MASS : m/z = 378 (M+H)<sup>+</sup>

15 Preparation 77

Methyl 4-[4-(5-phenoxy-pentyloxy)phenyl]benzoate

IR (KBr) : 2944, 2931, 1720, 1600, 1492, 1197,  
1110 cm<sup>-1</sup>

20 NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.6-1.8 (2H, m), 1.8-2.0 (4H, m),  
3.93 (3H, s), 4.00 (2H, t, J=6.3Hz), 4.04 (2H, t,  
J=6.3Hz), 6.9-7.1 (5H, m), 7.3-7.4 (2H, m), 7.56  
(2H, d, J=8.7Hz), 7.62 (2H, d, J=8.3Hz), 8.07 (2H,  
d, J=8.3Hz)  
APCI-MASS : m/z = 391 (M+H)<sup>+</sup>

25

Preparation 78

1-[2-(4-Cyclohexylphenylamino)ethyl]-2-oxazolidone  
hydrochloride

IR (KBr) : 2923.6, 2852.2, 1747.2, 1683.6 cm<sup>-1</sup>

30 NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 1.1-1.5 (6H, m), 1.6-1.9 (4H, m),  
2.3-2.6 (1H, m), 3.3-3.5 (4H, m), 3.58 (2H, dd,  
J=9.4 and 7.4Hz), 4.22 (2H, dd, J=9.4 and 7.4Hz),  
7.1-7.4 (4H, m)

35 Preparation 79

77

08809723 05219  
261250 5260880



Methyl 4-[4-(8-hydroxyoctyloxy)phenyl]benzoate

IR (KBr) : 3250, 2933, 2856, 1724, 1602, 1436, 1292,  
1199  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.3-1.9 (12H, m), 3.6-3.8 (2H, br),  
3.93 (3H, s), 4.00 (2H, t,  $J=6.7\text{Hz}$ ), 4.82 (1H, s),  
7.68 (2H, d,  $J=8.7\text{Hz}$ ), 7.56 (2H, d,  $J=8.7\text{Hz}$ ), 7.62  
(2H, d,  $J=8.3\text{Hz}$ ), 8.07 (2H, d,  $J=8.3\text{Hz}$ )

APCI-MASS :  $m/z = 357$  ( $\text{M}+\text{H}^+$ )

10 Preparation 80

Methyl 4-[4-(6-bromohexyloxy)phenyl]benzoate

IR (KBr) : 2937, 2861, 1724, 1602, 1529, 1436, 1292,  
1199, 1112  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.5-2.0 (8H, m), 3.43 (2H, t,  
 $J=6.8\text{Hz}$ ), 3.93 (3H, s), 4.02 (2H, t,  $J=6.3\text{Hz}$ ), 6.98  
(2H, d,  $J=8.8\text{Hz}$ ), 7.56 (2H, d,  $J=8.8\text{Hz}$ ), 7.62 (2H,  
d,  $J=8.4\text{Hz}$ ), 8.07 (2H, d,  $J=8.4\text{Hz}$ )

APCI-MASS :  $m/z = 391$  ( $\text{M}+\text{H}^+$ )

20 Preparation 81

4-[4-(5-Bromopentyloxy)phenyl]bromobenzene

IR (KBr) : 2942, 2867, 1604, 1515, 1477, 1286  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.5-2.0 (6H, m), 3.44 (2H, t,  
 $J=6.7\text{Hz}$ ), 3.99 (2H, t,  $J=6.2\text{Hz}$ ), 6.95 (2H, d,  
 $J=8.7\text{Hz}$ ), 7.3-7.6 (6H, m)

APCI-MASS :  $m/z = 399$  ( $\text{M}+\text{H}^+$ )

Preparation 82

8-[4-(4-Methoxycarbonylphenyl)phenoxy]octanoyl  
piperidine

IR (KBr) : 2935, 2852, 1720, 1639, 1604, 1438,  
1292  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.3-1.9 (16H, m), 2.34 (2H, d,  
 $J=7.6\text{Hz}$ ), 3.4-3.6 (4H, m), 3.93 (3H, s), 3.99 (2H,  
t,  $J=6.4\text{Hz}$ ), 6.97 (2H, d,  $J=8.8\text{Hz}$ ), 7.55 (2H, d,

J=8.8Hz), 7.61 (2H, d, J=8.6Hz), 8.07 (2H, d, J=8.6Hz)

APCI-MASS : m/z = 438 (M+H<sup>+</sup>)

5 Preparation 83

Methyl 6-[4-(4-n-heptyloxyphenyl)piperazin-1-yl]nicotinate

IR (KBr) : 2933, 2859, 1726, 1608, 1513, 1430, 1280, 1245 cm<sup>-1</sup>

10 NMR (CDCl<sub>3</sub>, δ) : 0.89 (3H, t, J=6.7Hz), 1.2-1.8 (10H, m), 3.17 (4H, t, J=4.9Hz), 3.8-4.0 (9H, m), 6.65 (1H, d, J=9.1Hz), 6.86 (2H, d, J=9.1Hz), 6.96 (2H, d, J=9.1Hz), 8.05 (1H, dd, J=9.1 and 2.3Hz), 8.82 (1H, d, J=2.3Hz)

15 APCI-MASS : m/z = 412 (M+H<sup>+</sup>)

Preparation 84

Methyl 6-[4-[4-(8-bromooctyloxy)phenyl]piperazin-1-yl]nicotinate

20 IR (KBr) : 2933, 2861, 1724, 1608, 1513, 1430, 1280 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 1.2-2.0 (12H, m), 3.17 (4H, t, J=5.0Hz), 3.40 (2H, t, J=6.8Hz), 3.8-4.0 (9H, m), 6.64 (1H, d, J=9.0Hz), 6.85 (2H, d, J=9.1Hz), 6.96 (2H, d, J=9.1Hz), 8.05 (1H, dd, J=9.0 and 2.2Hz), 8.82 (1H, d, J=2.2Hz)

25 APCI-MASS : m/z = 504 (M+H<sup>+</sup>)

Preparation 85

30 4-[4-(7-Bromoheptyloxy)phenyl]bromobenzene

IR (KBr) : 2935.1, 2856.1, 1604.5 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 1.18-1.65 (6H, m), 1.70-2.02 (4H, m), 3.41 (2H, t, J=6.8Hz), 3.99 (2H, t, J=6.4Hz), 6.95 (2H, d, J=8.6Hz), 7.40 (2H, d, J=8.6Hz), 7.46 (2H, d, J=8.6Hz), 7.52 (2H, d, J=8.6Hz)

Preparation 86

4-[4-(8-Bromooctyloxy)phenyl]bromobenzene

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.22-1.65 (8H, m), 1.65-1.95 (4H, m),  
3.41 (2H, t, J=6.8Hz), 3.99 (2H, t, J=6.4Hz), 6.95  
(2H, d, J=8.6Hz), 7.40 (2H, d, J=8.6Hz), 7.46 (2H,  
d, J=8.6Hz), 7.52 (2H, d, J=8.6Hz)

Preparation 87

Methyl (E)-3-[4-[4-(5-hexenyloxy)phenyl]phenyl]acrylate

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.50-1.72 (2H, m), 1.72-1.95 (2H, m),  
2.05-2.14 (2H, m), 3.82 (3H, s), 4.01 (2H, t,  
J=6.3Hz), 4.95-5.10 (2H, m), 5.70-5.93 (1H, m),  
6.46 (1H, d, J=16Hz), 6.97 (2H, d, J=8.7Hz), 7.54  
(2H, d, J=8.7Hz), 7.58 (4H, s), 7.72 (1H, d,  
J=16Hz)

APCI-MASS : m/z = 337 (M<sup>+</sup>+1)

Preparation 88

4-Bromo-4'-(4-methylpentyloxy)biphenyl

IR (KBr) : 2956.3, 2871.5, 1606.4 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.93 (6H, d, J=6.6Hz), 1.25-1.45 (2H,  
m), 1.62 (1H, sept, J=6.6Hz), 1.72-1.93 (2H, m),  
3.98 (2H, t, J=6.6Hz), 6.95 (2H, d, J=8.6Hz), 7.30-  
7.60 (6H, m)

APCI-MASS : m/z = 332, 334 (M<sup>+</sup>, M<sup>+</sup>+2)

The following compounds (Preparations 89 to 90) were  
obtained according to a similar manner to that of Preparation  
2.

Preparation 89

N-[4-[2-(4-Methylpentyl)-2,3-dihydro-4H-1,2,4-triazol-3-  
one-4-yl]phenyl]piperazine ditrifluoroacetate

IR (KBr) : 1668.1, 1519.6, 1203.4, 1176.4, 1130.1 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.86 (6H, d, J=6.6Hz), 1.1-1.3 (2H,

80

m), 1.4-1.8 (3H, m), 3.1-3.3 (4H, m), 3.3-3.5 (4H, m), 3.70 (2H, t, J=7.0Hz), 7.11 (2H, d, J=9.0Hz), 7.53 (2H, d, J=9.0Hz), 8.35 (1H, s), 8.90 (2H, s)

5 Preparation 90

1-(4-Phenylcyclohexyl)piperazine ditrifluoroacetate

IR (KBr) : 1677.8, 1197.6, 1133.9  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.4-1.8 (4H, m), 1.8-2.25 (4H, m),  
2.4-2.7 (1H, m), 3.2-3.7 (9H, m), 4.54 (2H, br s),  
7.0-7.4 (5H, m), 9.32 (1H, br s)

APCI-MASS :  $m/z$  = 245 ( $\text{M}^+ + \text{H}$ )

The following compounds (Preparations 91 to 103) were  
obtained according to a similar manner to that of Preparation  
3.

Preparation 91

Methyl 6-[4-(4-octyloxyphenyl)piperazin-1-yl]nicotinate

IR (KBr) : 2923, 1726, 1608, 1515, 1278, 1116  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.88 (3H, t, J=6.8Hz), 1.2-1.5 (10H, m),  
1.7-1.8 (2H, m), 3.1-3.2 (4H, m), 3.8-4.0 (9H, m), 6.64 (1H, d, J=9.0Hz), 6.8-7.0 (4H, m), 8.04  
(1H, dd, J=9.0 and 2.4Hz), 8.81 (1H, d, J=2.4Hz)

APCI-MASS :  $m/z$  = 426 ( $\text{M} + \text{H}^+$ )

Preparation 92

4-[4-[4-[2-(4-Methylpentyl)-2,3-dihydro-4H-1,2,4-triazol-3-one-4-yl]phenyl]piperazin-1-yl]benzonitrile

IR (KBr) : 2217.7, 1685.5  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (6H, d, J=6.6Hz), 1.2-1.4 (2H, m),  
1.5-2.0 (3H, m), 3.3-3.4 (4H, m), 3.4-3.6 (4H, m), 3.83 (2H, t, J=7.4Hz), 6.92 (2H, d, J=9.0Hz),  
7.01 (2H, d, J=9.0Hz), 7.43 (2H, d, J=9.0Hz), 7.54 (2H, d, J=9.0Hz), 7.62 (1H, s)

81

Preparation 93

3-Fluoro-4-[4-(4-methoxyphenyl)piperazin-1-yl]benzonitrile

IR (KBr) : 2225.5, 1510.0, 1240.0  $\text{cm}^{-1}$

5 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.1-3.55 (8H, m), 3.79 (3H, s),  
6.7-7.1 (6H, m), 7.3-7.5 (1H, m)

Preparation 94

10 3-Chloro-4-[4-(4-n-hexyloxyphenyl)piperazin-1-yl]benzonitrile

IR (KBr) : 2223.5, 1592.9, 1510.0, 1490.7, 1236.1  $\text{cm}^{-1}$

15 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.7\text{Hz}$ ), 1.3-1.6 (6H, m), 1.7-1.9 (2H, m), 3.2-3.4 (8H, m), 3.92 (2H, t,  $J=6.6\text{Hz}$ ), 6.85 (2H, d,  $J=9.3\text{Hz}$ ), 6.94 (2H, d,  $J=9.3\text{Hz}$ ), 7.08 (1H, d,  $J=8.4\text{Hz}$ ), 7.53 (1H, dd,  $J=8.4$  and  $1.9\text{Hz}$ ), 7.64 (1H, d,  $J=1.9\text{Hz}$ )

APCI-MASS :  $m/z$  = 398 ( $M^+ + H$ )

Preparation 95

20 Ethyl 3-[4-(4-n-hexyloxyphenyl)piperazin-1-yl]-6-pyridazinecarboxylate

IR (KBr) : 1729.8, 1587.1, 1511.9, 1245.8  $\text{cm}^{-1}$

25 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.5\text{Hz}$ ), 1.2-1.4 (6H, m), 1.44 (3H, t,  $J=7.1\text{Hz}$ ), 1.65-1.85 (2H, m), 3.1-3.25 (4H, m), 3.8-4.0 (6H, m), 4.46 (2H, q,  $J=7.1\text{Hz}$ ), 6.8-7.0 (5H, m), 7.91 (1H, d,  $J=9.6\text{Hz}$ )

APCI-MASS :  $m/z$  = 413 ( $M^+ + H$ )

Preparation 96

4-(4-Piperidinopiperidin-1-yl)benzonitrile

30 IR (KBr) : 2217.7, 1602.6, 1511.9  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.35-1.75 (8H, m), 1.92 (2H, d,  $J=12.9\text{Hz}$ ), 2.3-2.6 (5H, m), 2.86 (2H, td,  $J=12.8$  and  $2.6\text{Hz}$ ), 3.90 (2H, d,  $J=12.8\text{Hz}$ ), 6.84 (2H, d,  $J=9.1\text{Hz}$ ), 7.46 (2H, d,  $J=9.1\text{Hz}$ )

35 APCI-MASS :  $m/z$  = 270 ( $M^+ + H$ )

82

08009723.052197  
267250"2260880

Preparation 97

5-[4-(4-n-Hexyloxyphenyl)piperazin-1-yl]picolinonitrile

IR (KBr) : 2223.5, 1575.6, 1511.9, 1241.9  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.5\text{Hz}$ ), 1.2-1.55 (6H, m), 1.7-1.85 (2H, m), 3.22 (4H, t,  $J=5.1\text{Hz}$ ), 3.52 (4H, t,  $J=5.1\text{Hz}$ ), 3.92 (2H, t,  $J=6.5\text{Hz}$ ), 6.86 (2H, d,  $J=9.4\text{Hz}$ ), 6.93 (2H, d,  $J=9.4\text{Hz}$ ), 7.13 (1H, dd,  $J=8.8$  and  $3.0\text{Hz}$ ), 7.53 (1H, d,  $J=8.8\text{Hz}$ ), 8.35 (1H, d,  $J=3.0\text{Hz}$ )

APCI-MASS :  $m/z = 365$  ( $M^+ + H$ )

Preparation 98

4-[4-(4-Cyclohexylphenyl)piperazin-1-yl]benzonitrile

IR (KBr) : 2219.7, 1606.4, 1513.8, 1238.1  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.1-1.5 (6H, m), 1.65-2.0 (4H, m), 2.44 (1H, m), 3.30 (4H, t,  $J=5.1\text{Hz}$ ), 3.46 (4H, t,  $J=5.1\text{Hz}$ ), 6.90 (4H, d,  $J=8.9\text{Hz}$ ), 7.14 (2H, d,  $J=8.9\text{Hz}$ ), 7.52 (2H, d,  $J=8.9\text{Hz}$ )

APCI-MASS :  $m/z = 346$  ( $M^+ + H$ )

Preparation 99

4-[4-(4-n-Hexylphenyl)piperazin-1-yl]benzonitrile

IR (KBr) : 2925.5, 2850.3, 2213.9, 1604.5, 1513.8, 1234.2, 944.9  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.4\text{Hz}$ ), 1.2-1.45 (6H, m), 1.45-1.7 (2H, m), 2.54 (2H, t,  $J=7.6\text{Hz}$ ), 3.2-3.4 (4H, m), 3.4-3.6 (4H, m), 6.89 (2H, d,  $J=8.5\text{Hz}$ ), 6.91 (2H, d,  $J=8.9\text{Hz}$ ), 7.11 (2H, d,  $J=8.5\text{Hz}$ ), 7.52 (2H, d,  $J=8.9\text{Hz}$ )

Preparation 100

1-[2-(4-n-Hexylphenylamino)ethyl]-2-oxazolidone hydrochloride

IR (KBr) : 2925.5, 2852.2, 1753.0, 1729.8, 1267.0  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.5\text{Hz}$ ), 1.1-1.4 (6H, m)

43

m), 1.45-1.7 (2H, m), 2.56 (2H, t, J=7.6Hz), 3.3-3.53 (4H, m), 3.57 (2H, t, J=7.9Hz), 4.24 (2H, t, J=7.9Hz), 7.24 (4H, s)

APCI-MASS : m/z = 291 (M<sup>+</sup>+H)

5

Preparation 101

4-[4-(4-Phenylcyclohexyl)piperazin-1-yl]benzonitrile

IR (KBr) : 2212.0, 1602.6, 1513.8, 1249.6 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 1.3-1.8 (4H, m), 1.9-2.2 (4H, m), 2.3-2.6 (2H, m), 2.75 (4H, t, J=5.0Hz), 3.34 (4H, t, J=5.0Hz), 6.86 (2H, d, J=8.9Hz), 7.1-7.4 (5H, m), 7.49 (2H, d, J=8.9Hz)

10

APCI-MASS : m/z = 346 (M<sup>+</sup>+H)

15

Preparation 102

Methyl 6-[4-(4-hydroxyphenyl)piperazin-1-yl]nicotinate

IR (KBr) : 3411, 1691, 1602, 1510, 1432, 1249, 1147 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 3.0-3.1 (4H, m), 3.7-3.9 (7H, m), 6.67 (2H, d, J=8.8Hz), 6.84 (2H, d, J=8.8Hz), 6.93 (1H, d, J=9.1Hz), 7.97 (1H, dd, J=2.4 and 9.1Hz), 8.66 (1H, d, J=2.4Hz), 8.88 (1H, s)

20

APCI-MASS : m/z = 314 (M+H)<sup>+</sup>

25

Preparation 103

1-n-Decylindole-5-carboxylic acid

IR (KBr) : 2921, 2854, 1679, 1612, 1427, 1313, 1199 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.84 (3H, t, J=6.8Hz), 1.1-1.3 (14H, m), 1.6-1.8 (2H, m), 4.19 (2H, t, J=6.9Hz), 6.57 (1H, s), 7.4-7.8 (3H, m), 8.23 (1H, s), 12.40 (1H, s)

30

APCI-MASS : m/z = 302 (M+H<sup>+</sup>)

35

The following compounds (Preparations 104 to 111) were

84

08009723.052197  
267250.E2260880

obtained according to a similar manner to that of Preparation 10.

Preparation 104

5 (E)-Methyl 4-(4-n-butoxyphenyl)cinnamate

IR (KBr) : 2958, 2939, 2873, 1720, 1637, 1498, 1313,  
1195, 1170  $\text{cm}^{-1}$

10 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.98 (3H, t,  $J=7.3\text{Hz}$ ), 1.4-1.8 (4H, m), 3.81 (3H, s), 4.00 (2H, t,  $J=6.4\text{Hz}$ ), 6.45 (1H, d,  $J=16.0\text{Hz}$ ), 6.97 (2H, d,  $J=8.7\text{Hz}$ ), 7.5-7.7 (6H, m), 7.72 (1H, d,  $J=16.0\text{Hz}$ )

APCI-MASS :  $m/z = 311$  ( $M+H^+$ )

Preparation 105

15 Methyl (E)-3-[4-[4-(4-methylpentyloxy)phenyl]phenyl]-acrylate

IR (KBr) : 2956.3, 2873.4, 1720.2, 1635.3, 1600.6  $\text{cm}^{-1}$

20 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.93 (6H, d,  $J=6.5\text{Hz}$ ), 1.28-1.50 (2H, m), 1.50-1.95 (3H, m), 3.82 (3H, s), 3.99 (2H, t,  $J=6.6\text{Hz}$ ), 6.44 (1H, d,  $J=16.0\text{Hz}$ ), 6.97 (2H, d,  $J=8.7\text{Hz}$ ), 7.49-7.65 (6H, m), 7.71 (1H, d,  $J=16\text{Hz}$ )

APCI-MASS :  $m/z = 339$  ( $M^++1$ )

Preparation 106

25 Methyl (E)-3-[4-[4-(6-fluorohexyloxy)phenyl]phenyl]-acrylate

30 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.23-2.00 (8H, m), 3.81 (3H, s), 4.01 (2H, t,  $J=6.4\text{Hz}$ ), 4.47 (2H, dt,  $J=47.4$  and  $6.0\text{Hz}$ ), 6.45 (1H, d,  $J=16.0\text{Hz}$ ), 6.96 (2H, d,  $J=8.8\text{Hz}$ ), 7.45-7.63 (6H, m), 7.72 (1H, d,  $J=16.0\text{Hz}$ )

APCI-MASS :  $m/z = 357$  ( $M^++1$ )

Preparation 107

35 Methyl (E)-3-[4-[4-(6-methoxyhexyloxy)phenyl]phenyl]-

45

0809723.052197



acrylate

APCI-MASS :  $m/z = 369 (M^+)$

Preparation 108

5 Methyl (E)-3-[4-[4-(8-methoxyoctyloxy)phenyl]phenyl]-  
acrylate

IR (KBr) : 2935.1, 2858.0, 1722.1, 1637.3, 1602.6  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.30-1.70 (10H, m), 1.70-1.92 (2H, m), 3.33 (3H, s), 3.37 (2H, t,  $J=6.5\text{Hz}$ ), 3.81 (3H, s), 4.00 (2H, t,  $J=6.5\text{Hz}$ ), 6.45 (1H, d,  $J=16.0\text{Hz}$ ), 6.97 (2H, d,  $J=8.8\text{Hz}$ ), 7.46-7.78 (6H, m), 7.72 (1H, d,  $J=16.0\text{Hz}$ )

APCI-MASS :  $m/z = 397 (M^++1)$

15 Preparation 109

Methyl (E)-3-[4-(4-hydroxyphenyl)phenyl]acrylate

IR (KBr) : 3409.5, 1695.1  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 3.73 (3H, s), 6.64 (1H, d,  $J=16\text{Hz}$ ), 6.85 (2H, d,  $J=8.6\text{Hz}$ ), 7.50-7.83 (5H, m)

APCI-MASS :  $m/z = 255 (M^++1)$

Preparation 110

Methyl (E)-3-[4-[4-(7-methoxyheptyloxy)phenyl]phenyl]-  
acrylate

25 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.32-1.70 (8H, m), 1.70-1.92 (2H, m), 3.34 (3H, s), 3.38 (2H, t,  $J=6.4\text{Hz}$ ), 3.81 (3H, s), 4.00 (2H, t,  $J=6.5\text{Hz}$ ), 6.45 (1H, d,  $J=16.0\text{Hz}$ ), 6.97 (2H, d,  $J=8.8\text{Hz}$ ), 7.47-7.65 (6H, m), 7.70 (1H, d,  $J=16\text{Hz}$ )

30 APCI-MASS :  $m/z = 383 (M^++1)$

Preparation 111

Methyl (E)-3-[4-[4-(7-fluoroheptyloxy)phenyl]phenyl]-  
acrylate

35 IR (KBr) : 2937.1, 2861.8, 1722.1, 1637.3, 1600.6  $\text{cm}^{-1}$

46

0809723.052197  
261250.E260880

The following compound was obtained according to a similar manner to that of Preparation 20.

Preparation 112

5 Methyl 3-[4-(4-heptylphenyl)phenyl]propanoate

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.5\text{Hz}$ ), 1.15-1.50 (8H, m), 1.50-1.77 (2H, m), 2.52-2.73 (4H, m), 2.99 (2H, t,  $J=7.8\text{Hz}$ ), 3.68 (3H, s), 7.18-7.35 (4H, m), 7.40-7.58 (4H, m)

10 APCI-MASS :  $m/z = 339$  ( $M^++1$ )

The following compounds (Preparation 113 to 164) were obtained according to a similar manner to that of Preparation 32.

15

Preparation 113

4-(4-Octylphenyl)-2,4-dihydro-3H-1,2,4-triazol-3-one-2-yl-acetic acid

IR (KBr) : 2923.6, 1704.8, 1224.6  $\text{cm}^{-1}$

20

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.7\text{Hz}$ ), 1.1-1.4 (10H, m), 1.4-1.7 (2H, m), 2.60 (2H, t,  $J=7.2\text{Hz}$ ), 4.38 (2H, s), 7.32 (2H, d,  $J=8.5\text{Hz}$ ), 7.58 (2H, d,  $J=8.5\text{Hz}$ ), 8.43 (1H, s)

25

Preparation 114

1-Heptyl-4-(4-carboxyphenyl)pyrazole

IR (KBr) : 3106, 2917, 1687, 1612, 1425, 1295, 1184, 952, 860, 773  $\text{cm}^{-1}$

30

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.8\text{Hz}$ ), 1.1-1.4 (8H, m), 1.7-1.9 (2H, m), 4.11 (2H, t,  $J=7.0\text{Hz}$ ), 7.69 (2H, d,  $J=8.5\text{Hz}$ ), 7.91 (2H, d,  $J=8.5\text{Hz}$ ), 7.98 (1H, s), 8.32 (1H, s), 12.82 (1H, br)

APCI-MASS :  $m/z = 287$  ( $M+H^+$ )

35

Preparation 115

47

08809723.052197

6-[4-(4-Octyloxyphenyl)piperazin-1-yl]nicotinic acid

IR (KBr pelet) : 2919, 2854, 1697, 1608, 1515, 1429,  
1263, 1245, 1228  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.7\text{Hz}$ ), 1.1-1.5 (10H,  
m), 1.6-1.8 (2H, m), 3.0-3.2 (4H, m), 3.7-3.9 (4H,  
m), 3.88 (2H, t,  $J=6.4\text{Hz}$ ), 6.7-7.0 (5H, m), 7.95  
(1H, dd,  $J=9.0$  and  $1.1\text{Hz}$ ), 8.64 (1H, d,  $J=1.1\text{Hz}$ )

APCI-MASS :  $m/z = 412$  ( $\text{M}+\text{H}^+$ )

Preparation 116

2-(4-Hexyloxyphenyl)benzoxazole-5-carboxylic acid

IR (KBr) : 2952, 1689, 1677, 1619, 1500, 1415, 1299,  
1172, 1024  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.7\text{Hz}$ ), 1.2-1.5 (6H,  
m), 1.7-1.9 (2H, m), 4.09 (2H, t,  $J=6.5\text{Hz}$ ), 7.16  
(2H, d,  $J=8.8\text{Hz}$ ), 7.84 (1H, d,  $J=8.5\text{Hz}$ ), 8.01 (1H,  
dd,  $J=8.5$  and  $1.5\text{Hz}$ ), 8.15 (2H, d,  $J=8.8\text{Hz}$ ), 8.26  
(1H, d,  $J=1.5\text{Hz}$ )

APCI-MASS :  $m/z = 340$  ( $\text{M}+\text{H}^+$ )

Preparation 117

4-[4-(4-n-Butyloxyphenyl)phenyl]benzoic acid

IR (KBr) : 2958, 2873, 1689, 1600, 1537, 1396  $\text{cm}^{-1}$

Preparation 118

6-(4-Heptyloxyphenyl)nicotinic acid

IR (KBr) : 2858, 1699, 1674, 1589, 1425, 1180, 1016,  
781  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.7\text{Hz}$ ), 1.2-1.5 (8H,  
m), 1.6-1.8 (2H, m), 4.04 (2H, t,  $J=6.4\text{Hz}$ ), 7.06  
(2H, d,  $J=8.9\text{Hz}$ ), 8.03 (1H, d,  $J=8.2\text{Hz}$ ), 8.13 (2H,  
d,  $J=8.9\text{Hz}$ ), 8.27 (1H, dd,  $J=8.2$  and  $2.2\text{Hz}$ ), 9.09  
(1H, d,  $J=2.2\text{Hz}$ ), 13.31 (1H, br)

APCI-MASS :  $m/z = 314$  ( $\text{M}+\text{H}^+$ )

48

Preparation 119

5-(4-Octyloxyphenyl)isoxazole-3-carboxylic acid

IR (KBr pelet) : 2923, 2852, 1704, 1612, 1440, 1272,  
1178  $\text{cm}^{-1}$

5 NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.8\text{Hz}$ ), 1.2-1.6  
(10H, m), 1.6-1.9 (2H, m), 4.03 (2H, t,  $J=6.5\text{Hz}$ ),  
7.08 (2H, d,  $J=8.9\text{Hz}$ ), 7.25 (1H, s), 7.86 (2H, d,  
 $J=8.9\text{Hz}$ )

APCI-MASS :  $m/z = 318$  ( $\text{M}+\text{H}^+$ )

10

Preparation 120

2-(2-Octyloxypyridin-5-yl)benzoxazole-5-carboxylic acid

IR (KBr) : 2954, 2923, 2854, 1697, 1683, 1625, 1488,  
1290  $\text{cm}^{-1}$

15 NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=7.6\text{Hz}$ ), 1.2-1.5  
(10H, m), 1.7-1.8 (2H, m), 4.36 (2H, t,  $J=6.6\text{Hz}$ ),  
7.04 (1H, d,  $J=8.7\text{Hz}$ ), 7.88 (1H, d,  $J=8.5\text{Hz}$ ), 8.04  
(1H, dd,  $J=8.5$  and  $1.6\text{Hz}$ ), 8.29 (1H, d,  $J=1.6\text{Hz}$ ),  
8.43 (1H, dd,  $J=8.7$  and  $2.4\text{Hz}$ ), 8.99 (1H, d,  
20  $J=2.4\text{Hz}$ ), 13.0-13.2 (1H, br)

APCI-MASS :  $m/z = 369$  ( $\text{M}+\text{H}^+$ )

Preparation 121

2-[4-(4-Hexylphenyl)phenyl]benzoxazole-5-carboxylic acid

25 IR (KBr) : 2923, 2854, 1683, 1411, 1299, 1054  $\text{cm}^{-1}$

APCI-MASS :  $m/z = 400$  ( $\text{M}+\text{H}^+$ )

Preparation 122

6-[4-(4-n-Butyloxyphenyl)phenyl]nicotinic acid

30 IR (KBr) : 3406, 2958, 1691, 1591, 1394, 1284,  
1253  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.94 (3H, t,  $J=7.3\text{Hz}$ ), 1.4-1.8 (4H,  
m), 4.01 (2H, t,  $J=6.4\text{Hz}$ ), 7.02 (2H, d,  $J=8.7\text{Hz}$ ),  
7.57 (2H, d,  $J=8.7\text{Hz}$ ), 7.61 (2H, d,  $J=8.2\text{Hz}$ ), 7.83  
35 (2H, d,  $J=8.2\text{Hz}$ ), 8.05 (1H, d,  $J=8.5\text{Hz}$ ), 8.22 (1H,

89

0809723.052197

dd,  $J=8.5$  and  $1.6\text{Hz}$ ),  $9.14$  (1H, d,  $J=1.6\text{Hz}$ )  
APCI-MASS :  $m/z = 348$  ( $M+H^+$ )

Preparation 123

5 4-[4-(5-Phenoxypropyloxy)phenyl]benzoic acid

NMR (DMSO- $d_6$ ,  $\delta$ ) :  $1.5-1.7$  (2H, m),  $1.7-1.9$  (4H, m),  
 $3.98$  (2H, t,  $J=6.3\text{Hz}$ ),  $4.05$  (2H, t,  $J=6.1\text{Hz}$ ),  $6.8-$   
 $7.0$  (3H, m),  $7.05$  (2H, d,  $J=8.6\text{Hz}$ ),  $7.25$  (2H, t,  
 $J=8.2\text{Hz}$ ),  $7.68$  (2H, d,  $J=8.5\text{Hz}$ ),  $7.75$  (2H, d,  
10  $J=8.2\text{Hz}$ ),  $7.98$  (2H, d,  $J=8.2\text{Hz}$ ),  $12.8-13.0$  (1H, br  
s)

APCI-MASS :  $m/z = 375$  ( $M-H$ )<sup>-</sup>

Preparation 124

15 4-[5-(4-n-Hexyloxyphenyl)-1,3,4-oxadiazol-2-yl]benzoic  
acid

IR (KBr) :  $2935$ ,  $2854$ ,  $1685$ ,  $1612$ ,  $1495$ ,  $1425$ ,  $1286$ ,  
 $1251\text{ cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) :  $0.89$  (3H, t,  $J=6.7\text{Hz}$ ),  $1.2-1.5$  (6H,  
20 m),  $1.6-1.9$  (3H, m),  $4.12$  (2H, t,  $J=6.4\text{Hz}$ ),  $7.19$   
(2H, d,  $J=8.7\text{Hz}$ ),  $8.08$  (2H, d,  $J=8.7\text{Hz}$ ),  $8.18$  (2H,  
d,  $J=8.4\text{Hz}$ ),  $8.24$  (2H, d,  $J=8.4\text{Hz}$ )

APCI-MASS :  $m/z = 367$  ( $M+H$ )<sup>+</sup>

25 Preparation 125

4-[5-(4-n-Hexyloxyphenyl)-1,3,4-thiadiazol-2-yl]benzoic  
acid

IR (KBr) :  $2952$ ,  $2586$ ,  $1699$ ,  $1604$ ,  $1517$ ,  $1432$ ,  $1251$ ,  
 $1174\text{ cm}^{-1}$

30 NMR (DMSO- $d_6$ ,  $\delta$ ) :  $0.89$  (3H, t,  $J=6.7\text{Hz}$ ),  $1.3-1.9$  (8H,  
m),  $4.04$  (2H, t,  $J=6.3\text{Hz}$ ),  $7.13$  (2H, d,  $J=8.8\text{Hz}$ ),  
 $7.97$  (2H, d,  $J=8.8\text{Hz}$ ),  $8.11$  (4H, s)

APCI-MASS :  $m/z = 383$  ( $M+H$ )<sup>+</sup>

35 Preparation 126

5-(4-Octyloxyphenyl)-1-methylpyrazole-3-carboxylic acid

IR (KBr pelet) : 2950, 2923, 1695, 1450, 1282, 1251,  
956  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.8\text{Hz}$ ), 1.2-1.5  
(10H, m), 1.6-1.8 (2H, m), 3.98 (2H, t,  $J=6.5\text{Hz}$ ),  
4.10 (3H, s), 6.95 (1H, d,  $J=8.8\text{Hz}$ ), 7.18 (1H, s),  
7.73 (2H, d,  $J=8.8\text{Hz}$ ), 13.37 (1H, br)

APCI-MASS :  $m/z = 331$  ( $\text{M}+\text{H}^+$ )

10 Preparation 127

4-[3-(4-n-Pentyloxyphenyl)pyrazol-5-yl]benzoic acid

IR (KBr) : 3224, 2956, 1692, 1614, 1506, 1251  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.91 (3H, t,  $J=6.9\text{Hz}$ ), 1.3-1.5 (4H,  
m), 1.6-1.8 (2H, m), 4.00 (2H, t,  $J=6.5\text{Hz}$ ), 7.02  
(2H, d,  $J=8.8\text{Hz}$ ), 7.19 (1H, s), 7.75 (2H, d,  
 $J=8.8\text{Hz}$ ), 7.95 (2H, d,  $J=8.7\text{Hz}$ ), 8.02 (2H, d,  
 $J=8.7\text{Hz}$ ), 12.8-13.3 (2H, br)

APCI-MASS :  $m/z = 351$  ( $\text{M}+\text{H}^+$ )

20 Preparation 128

5-[4-(4-n-Butoxyphenyl)phenyl]furan-2-carboxylic acid

IR (KBr) : 2958, 2873, 1679, 1487, 1253, 1166  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.95 (3H, t,  $J=7.3\text{Hz}$ ), 1.3-1.8 (4H,  
m), 4.02 (2H, t,  $J=6.3\text{Hz}$ ), 7.03 (2H, d,  $J=8.6\text{Hz}$ ),  
7.17 (1H, d,  $J=3.6\text{Hz}$ ), 7.33 (1H, d,  $J=3.6\text{Hz}$ ), 7.66  
(2H, d,  $J=8.6\text{Hz}$ ), 7.74 (2H, d,  $J=8.4\text{Hz}$ ), 7.86 (2H,  
d,  $J=8.4\text{Hz}$ ), 13.1 (1H, br s)

APCI-MASS :  $m/z = 337$  ( $\text{M}+\text{H}^+$ )

30 Preparation 129

3-(S)-Hydroxyhexadecanoic acid

IR (KBr) : 1679.7, 1467.6, 1224.6  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.4\text{Hz}$ ), 1.1-1.7 (24H,  
m), 2.35-2.65 (2H, m), 4.03 (1H, m), 5.41 (1H, br  
s)

91

Preparation 130

6-[4-(4-n-Hexyloxyphenyl)piperazin-1-yl]pyridazine-3-carboxylic acid

IR (KBr) : 1697.1, 1589.1, 1515.8, 1448.3  $\text{cm}^{-1}$

5 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.4\text{Hz}$ ), 1.2-1.5 (6H, m), 1.6-1.8 (2H, m), 3.0-3.2 (4H, m), 3.7-4.0 (6H, m), 6.83 (2H, d,  $J=9.0\text{Hz}$ ), 6.95 (2H, d,  $J=9.0\text{Hz}$ ), 7.36 (1H, d,  $J=9.6\text{Hz}$ ), 7.86 (1H, d,  $J=9.6\text{Hz}$ ), 11.68 (1H, s)

10

Preparation 131

4-[4-[1-(4-n-Hexyloxyphenyl)piperidin-4-yl]piperazin-1-yl]benzoic acid hydrochloride

IR (KBr) : 1699.0, 1608.3, 1513.8  $\text{cm}^{-1}$

15 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.5\text{Hz}$ ), 1.2-1.5 (6H, m), 1.6-1.8 (2H, m), 2.0-2.45 (3H, m), 3.2-3.8 (12H, m), 3.94 (2H, t,  $J=6.4\text{Hz}$ ), 4.03 (2H, d,  $J=11\text{Hz}$ ), 6.95 (2H, d,  $J=8.7\text{Hz}$ ), 7.07 (2H, d,  $J=8.9\text{Hz}$ ), 7.32 (2H, br s), 7.83 (2H, d,  $J=8.9\text{Hz}$ )

20 APCI-MASS :  $m/z = 466$  ( $\text{M}^+ + \text{H}$ )

Preparation 132

6-(8-Methoxyoctyloxy)-2-naphthoic acid

IR (KBr) : 2937.1, 2854.1, 1677.8, 1211.1  $\text{cm}^{-1}$

25 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.2-1.6 (10H, m), 1.7-1.9 (2H, m), 3.20 (3H, s), 3.29 (2H, t,  $J=6.5\text{Hz}$ ), 4.11 (2H, t,  $J=6.4\text{Hz}$ ), 7.23 (1H, dd,  $J=9.0$  and  $2.3\text{Hz}$ ), 7.39 (1H, d,  $J=2.3\text{Hz}$ ), 7.85 (1H, d,  $J=8.7\text{Hz}$ ), 7.93 (1H, d,  $J=8.7\text{Hz}$ ), 7.99 (1H, d,  $J=9.0\text{Hz}$ ), 8.51 (1H, s), 12.9 (1H, s)

30

Preparation 133

Mixture of (E) and (Z)-3-[4-(4-Heptylphenyl)phenyl]-2-butenic acid

35 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.6\text{Hz}$ ), 1.15-1.50 (8H,

92

08809723.052197

m), 1.52-1.75 (2H, m), 2.63 and 3.62 (total 3H, each s), 2.53-2.75 (2H, m), 6.24 and 5.68 (total 1H, each s), 7.19-7.35 (2H, m), 7.47-7.70 (6H, m)  
APCI-MASS : m/z = 337 ( $M^+ + 1$ ), 351 (methyl ester $^+ + 1$ )

5

Preparation 134

3-[4-(4-Heptylphenyl)phenyl]propanoic acid

NMR ( $CDCl_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.6$ Hz), 1.13-1.48 (8H, m), 1.48-1.75 (2H, m), 2.52-2.83 (4H, m), 3.00 (2H, t,  $J=7.8$ Hz), 7.15-7.35 (4H, m), 7.40-7.60 (4H, m)

10

APCI-MASS : m/z = 323 ( $M^+ - 1$ )

Preparation 135

4-(4-n-Heptylphenyl)benzoyl-carboxylic acid

NMR ( $CDCl_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.6$ Hz), 1.13-1.50 (8H, m), 1.50-1.75 (2H, m), 2.66 (2H, t,  $J=7.7$ Hz), 7.20-7.40 (2H, m), 7.50-7.66 (2H, m), 7.66-7.84 (2H, m), 8.40-8.60 (2H, m)

15

APCI-MASS : m/z = 323 ( $M^+ - 1$ )

20

Preparation 136

6-Hexylnaphthalene-2-carboxylic acid

NMR ( $CDCl_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.8$ Hz), 1.15-1.53 (6H, m), 1.55-1.84 (2H, m), 2.80 (2H, t,  $J=7.6$ Hz), 7.42 (1H, dd,  $J=1.7$  and 8.4Hz), 7.67 (1H, s), 7.84 (1H, d,  $J=8.6$ Hz), 7.90 (1H, d,  $J=8.4$ Hz), 8.09 (1H, dd,  $J=1.7$  and 8.6Hz), 8.68 (1H, s)

25

APCI-MASS : m/z = 257 ( $M^+ + 1$ ), 271 (methyl ester $^+ + 1$ )

30

Preparation 137

3-(E)-[4-[4-(7-Methoxyheptyloxy)phenyl]phenyl]acrylic acid

NMR ( $DMSO-d_6$ ,  $\delta$ ) : 1.20-1.60 (8H, m), 1.60-1.83 (2H, m), 3.21 (3H, s), 3.25-3.60 (2H, m), 4.01 (2H, t,  $J=6.4$ Hz), 6.54 (1H, d,  $J=16.0$ Hz), 7.02 (2H, d,

35

93

0809723.052497  
26 FEB 90 12:26:00



J=8.8Hz), 7.55-7.80 (7H, m)

APCI-MASS : m/z = 369 ( $M^+$ +1)

Preparation 138

5        3-(E)-[4-[4-(8-Methoxyoctyloxy)phenyl]phenyl]acrylic  
acid

IR (KBr) : 3037.3, 2933.2, 2858.0, 2551.4, 1706.7,  
1677.8, 1629.6, 1602.6  $\text{cm}^{-1}$

10        NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.18-1.55 (10H, m), 1.65-1.83 (2H,  
m), 3.18-3.45 (5H, m), 4.01 (2H, t, J=6.5Hz), 6.53  
(1H, d, J=16.0Hz), 7.02 (2H, d, J=8.8Hz), 7.50-8.80  
(7H, m)

APCI-MASS : m/z = 383 ( $M^+$ +1)

15        Preparation 139

3-(E)-[4-[4-(5-Hexenyloxy)phenyl]phenyl]acrylic acid

20        NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.42-1.63 (2H, m), 1.63-1.85 (2H,  
m), 2.00-2.20 (2H, m), 4.03 (2H, t, J=6.3Hz), 4.90-  
5.15 (2H, m), 5.68-5.97 (1H, m), 6.54 (1H, d,  
J=16Hz), 7.02 (2H, d, J=8.7Hz), 7.50-7.80 (7H, m)

APCI-MASS : m/z = 323 ( $M^+$ +1)

Preparation 140

25        3-(E)-[4-[4-(4-Methylpentyloxy)phenyl]phenyl]acrylic  
acid

IR (KBr) : 2956.3, 2869.6, 2713.4, 2599.6, 1689.3,  
1627.6, 1602.6  $\text{cm}^{-1}$

30        NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (6H, d, J=6.5Hz), 1.15-1.43  
(2H, m), 1.48-1.90 (3H, m), 4.00 (2H, t, J=6.7Hz),  
6.54 (1H, d, J=16Hz), 7.02 (2H, d, J=8.7Hz), 7.50-  
7.90 (7H, m)

APCI-MASS : m/z = 325 ( $M^+$ +1)

Preparation 141

35        3-(E)-[4-[4-(6-Fluorohexyloxy)phenyl]phenyl]acrylic acid

94

08809723 052197  
267250 E2/60880

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.39-2.00 (8H, m), 4.01 (2H, t, J=6.5Hz), 4.47 (2H, dt, J=47.3 and 6.0Hz), 6.49 (1H, d, J=15.9Hz), 6.98 (2H, d, J=8.7Hz), 7.40-7.70 (6H, m), 7.81 (1H, d, J=15.9Hz)

5 APCI-MASS : m/z = 343 (M<sup>+</sup>+1)

Preparation 142

3-(E)-[4-[4-(6-Methoxyhexyloxy)phenyl]phenyl]acrylic acid

10 NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 1.22-1.63 (6H, m), 1.63-1.88 (2H, m), 3.21 (3H, s), 3.22-3.40 (2H, m), 4.00 (2H, t, J=6.5Hz), 6.54 (1H, d, J=15.8Hz), 7.02 (2H, d, J=8.7Hz), 7.50-7.84 (7H, m)

APCI-MASS : m/z = 369 (methyl ester, M<sup>+</sup>+1)

15

Preparation 143

4-[4-[8-(Tetrahydropyran-2-yl-oxy)octyloxy]phenyl]benzoic acid

20 IR (KBr) : 2935, 1697, 1683, 1604, 1303, 1290, 1197 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 1.2-1.8 (18H, m), 3.3-3.9 (4H, m), 4.01 (2H, t, J=6.3Hz), 4.5-4.6 (1H, m), 7.03 (2H, d, J=8.7Hz), 7.67 (2H, d, J=8.7Hz), 7.74 (2H, d, J=8.3Hz), 7.98 (2H, d, J=8.3Hz)

25 APCI-MASS : m/z = 425 (M-H<sup>+</sup>)

Preparation 144

4-[3-(4-n-Hexyloxyphenyl)pyrazol-5-yl]benzoic acid

30 IR (KBr) : 2956, 2935, 1693, 1614, 1508, 1432, 1251, 1178 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.89 (3H, t, J=6.4Hz), 1.2-1.5 (6H, m), 1.6-1.8 (2H, m), 4.00 (2H, t, J=6.4Hz), 7.02 (2H, d, J=8.7Hz), 7.12 (1H, s), 7.74 (2H, d, J=8.7Hz), 7.95 (2H, d, J=8.8Hz), 8.01 (2H, d, J=8.8Hz), 13.17 (1H, s)

35

95

0809723.052497  
26 FEB 90 12:22:00

APCI-MASS :  $m/z = 365$  ( $M+H^+$ )

Preparation 145

4-[4-[4-(6-Methoxyhexyloxy)phenyl]phenyl]benzoic acid

5 IR (KBr) : 2939, 2861, 1685, 1602, 1430, 1286,  
1128  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.3-1.8 (8H, m), 3.21 (3H, s),  
3.3-3.4 (2H, m), 4.01 (2H, t,  $J=6.5\text{Hz}$ ), 7.04 (2H,  
d,  $J=8.6\text{Hz}$ ), 7.66 (2H, d,  $J=8.6\text{Hz}$ ), 7.7-7.9 (6H,  
10 m), 8.03 (2H, d,  $J=8.2\text{Hz}$ )

APCI-MASS :  $m/z = 405$  ( $M+H^+$ )

Preparation 146

15 4-[5-[4-(8-Methoxyoctyloxy)phenyl]-1,3,4-thiadiazol-2-  
yl]benzoic acid

IR (KBr) : 2931, 2854, 1691, 1602, 1251  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.2-2.0 (12H, m), 3.20 (3H, s),  
3.29 (2H, t,  $J=6.4\text{Hz}$ ), 4.04 (2H, t,  $J=6.4\text{Hz}$ ), 7.13  
(2H, t,  $J=8.8\text{Hz}$ ), 7.9-8.2 (6H, m), 13.95 (1H, br)

20 APCI-MASS :  $m/z = 441$  ( $M+H^+$ )

Preparation 147

4-(4-n-Butoxyphenyl)cinnamic acid

IR (KBr) : 2958, 2871, 1695, 1625, 1498, 1249  $\text{cm}^{-1}$

25 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.94 (3H, t,  $J=7.3\text{Hz}$ ), 1.44 (2H,  
tq,  $J=7.0$  and  $7.3\text{Hz}$ ), 1.71 (2H, tt,  $J=7.0$  and  
6.4Hz), 4.01 (2H, t,  $J=6.4\text{Hz}$ ), 6.54 (1H, d,  
 $J=16.0\text{Hz}$ ), 7.02 (2H, d,  $J=8.7\text{Hz}$ ), 7.6-7.9 (7H, m)

APCI-MASS :  $m/z = 297$  ( $M+H^+$ )

Preparation 148

4-[5-(4-Cyclohexylphenyl)-1,3,4-thiadiazol-2-yl]benzoic  
acid

IR (KBr) : 2925, 2850, 1683, 1429, 1292  $\text{cm}^{-1}$

35 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.1-1.5 (5H, m), 1.6-2.0 (5H, m),

96

08809723 052197  
267250 E260880

2.4-2.6 (1H, m), 7.45 (2H, d, J=8.3Hz), 7.96 (2H, d, J=8.3Hz), 8.13 (4H, s)  
APCI-MASS : m/z = 365 (M+H)<sup>+</sup>

5 Preparation 149

4-[5-[4-(Piperidin-1-yl)phenyl]-1,3,4-thiadiazol-2-yl]-benzoic acid

IR (KBr) : 2931, 2854, 1685, 1604, 1415, 1238 cm<sup>-1</sup>

10 NMR (DMSO-d<sub>6</sub>, δ) : 1.61 (6H, s), 3.31 (4H, s), 7.05 (2H, d, J=9.0Hz), 7.83 (2H, d, J=9.0Hz), 8.10 (4H, s)

APCI-MASS : m/z = 366 (M+H)<sup>+</sup>

Preparation 150

15 4-[5-[4-[4-n-Propyloxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoic acid

IR (KBr) : 2939, 1689, 1606, 1488, 1429, 1290 cm<sup>-1</sup>

20 NMR (DMSO-d<sub>6</sub>, δ) : 1.00 (3H, t, J=7.3Hz), 1.76 (2H, tq, J=6.5 and 7.3Hz), 4.00 (2H, t, J=6.5Hz), 7.07 (2H, d, J=8.8Hz), 7.70 (2H, d, J=8.5Hz), 7.78 (2H, d, J=8.8Hz), 7.90 (2H, d, J=8.5Hz), 8.0-8.4 (4H, m)

APCI-MASS : m/z = 401 (M+H)<sup>+</sup>

Preparation 151

25 4-(5-n-Nonyl-1,3,4-oxadiazol-2-yl)benzoic acid

IR (KBr) : 2919, 2852, 1685, 1565, 1430, 1284 cm<sup>-1</sup>

30 NMR (DMSO-d<sub>6</sub>, δ) : 0.84 (3H, t, J=6.5Hz), 1.2-1.5 (12H, m), 1.7-1.9 (2H, m), 2.94 (2H, t, J=7.4Hz), 8.0-8.2 (4H, m), 13.35 (1H, s)

APCI-MASS : m/z = 317 (M+H)<sup>+</sup>

Preparation 152

35 4-[3-(4-n-Hexyloxyphenyl)-1,2,4-oxadiazol-5-yl]benzoic acid

IR (KBr) : 2942, 2869, 1695, 1421, 1251 cm<sup>-1</sup>

97

08809723, 052197  
267250, E2760880

NMR (DMSO-d<sub>6</sub>, δ) : 0.89 (3H, t, J=6.8Hz), 1.2-1.8 (8H, m), 4.06 (2H, t, J=6.5Hz), 7.13 (2H, d, J=8.9Hz), 8.03 (2H, d, J=8.9Hz), 8.17 (2H, d, J=8.5Hz), 8.28 (2H, d, J=8.5Hz)

5 APCI-MASS : m/z = 367 (M+H)<sup>+</sup>

Preparation 153

4-[4-[4-(5-Methoxypentyloxy)phenyl]phenyl]phenylacetic acid

10 IR (KBr) : 2939, 2861, 1699, 1253, 1182, 1124 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.4-1.9 (6H, m), 3.22 (3H, s), 3.39 (2H, t, J=6.2Hz), 3.61 (2H, s), 4.01 (2H, t, J=6.4Hz), 7.02 (2H, d, J=8.8Hz), 7.35 (2H, d, J=8.2Hz), 7.6-7.8 (8H, m)

15 APCI-MASS : m/z = 405 (M+H)<sup>+</sup>

Preparation 154

4-[5-(4-n-Octyloxyphenyl)-1,3,4-thiadiazol-2-yl]benzoic acid

20 IR (KBr) : 2921, 2856, 1691, 1432, 1251 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.87 (3H, t, J=6.7Hz), 1.2-1.5 (10H, m), 1.7-1.9 (2H, m), 4.07 (2H, t, J=6.5Hz), 7.13 (2H, d, J=8.9Hz), 7.97 (2H, d, J=8.9Hz), 8.12 (4H, s)

25 APCI-MASS : m/z = 411 (M+H)<sup>+</sup>

Preparation 155

4-[5-(4-Trans-n-pentylcyclohexyl)-1,3,4-thiadiazol-2-yl]benzoic acid

30 IR (KBr) : 2919, 2848, 1677, 1430, 1294 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.87 (3H, t, J=6.9Hz), 1.0-1.4 (11H, m), 1.5-1.6 (2H, m), 1.8-2.0 (2H, m), 2.1-2.3 (2H, m), 3.1-3.3 (1H, m), 8.07 (4H, s)

APCI-MASS : m/z = 359 (M+H)<sup>+</sup>

35

98

0809723 052197  
267250 E260880

Preparation 156

4-[3-(4-n-Pentyloxyphenyl)isoxazol-5-yl]benzoic acid

IR (KBr) : 2925, 2869, 1699, 1687, 1612, 1432, 1251,  
1178  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.91 (3H, t,  $J=6.9\text{Hz}$ ), 1.2-1.5 (4H,  
m), 1.7-1.9 (2H, m), 4.04 (2H, t,  $J=6.5\text{Hz}$ ), 7.09  
(2H, d,  $J=8.8\text{Hz}$ ), 7.69 (1H, s), 7.85 (2H, d,  
 $J=8.8\text{Hz}$ ), 8.01 (2H, d,  $J=8.5\text{Hz}$ ), 8.11 (2H, d,  
 $J=8.5\text{Hz}$ )

APCI-MASS :  $m/z = 352$  ( $M+H^+$ )

Preparation 157

4-[5-[4-(8-Methoxyoctyloxy)phenyl]-1,3,4-oxadiazol-2-  
yl]benzoic acid

IR (KBr) : 2967, 2937, 2877, 1687, 1290  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 1.2-1.6 (10H, m), 1.7-1.9 (2H, m),  
3.20 (3H, s), 3.29 (2H, t,  $J=6.4\text{Hz}$ ), 4.08 (2H, t,  
 $J=6.5\text{Hz}$ ), 7.17 (2H, d,  $J=8.9\text{Hz}$ ), 8.07 (2H, d,  
 $J=8.9\text{Hz}$ ), 8.15 (2H, d,  $J=8.6\text{Hz}$ ), 8.24 (2H, d,  
 $J=8.6\text{Hz}$ )

APCI-MASS :  $m/z = 425$  ( $M+H$ )<sup>+</sup>

Preparation 158

4-[4-(6-Phenylpyridazin-3-yl-oxy)phenyl]benzoic acid

IR (KBr) : 1700, 1687, 1608, 1427, 1284, 1186  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 7.40 (2H, d,  $J=8.6\text{Hz}$ ), 7.5-7.7 (4H,  
m), 7.7-7.9 (4H, m), 7.9-8.1 (4H, m), 8.35 (1H, d,  
 $J=9.2\text{Hz}$ ), 12.99 (1H, br s)

APCI-MASS :  $m/z = 369$  ( $M+H$ )<sup>+</sup>

Preparation 159

4-[5-(4-n-Octyloxyphenyl)-1,3,4-oxadiazol-2-yl]benzoic  
acid

IR (KBr) : 2921, 2852, 1685, 1612, 1496, 1425, 1288,  
1251  $\text{cm}^{-1}$

99

NMR (DMSO-d<sub>6</sub>, δ) : 0.87 (3H, t, J=6.7Hz), 1.2-1.5  
(10H, m), 1.7-1.9 (2H, m), 4.08 (2H, t, J=6.4Hz),  
7.17 (2H, d, J=8.7Hz), 8.07 (2H, d, J=8.7Hz), 8.15  
(2H, d, J=8.5Hz), 8.24 (2H, d, J=8.5Hz), 13.36 (1H,  
br)  
APCI-MASS : m/z = 395 (M+H<sup>+</sup>)

Preparation 160

4-[2-(4-n-Hexyloxyphenyl)pyrimidin-6-yl]benzoic acid

IR (KBr) : 2944, 2863, 1697, 1585, 1415, 1386,  
1253 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.89 (3H, t, J=6.7Hz), 1.2-1.6 (6H,  
m), 1.7-1.9 (2H, m), 4.07 (2H, t, J=6.6Hz), 7.10  
(2H, d, J=8.9Hz), 8.00 (1H, d, J=5.2Hz), 8.13 (2H,  
d, J=8.4Hz), 8.44 (2H, d, J=5.9Hz), 8.47 (2H, d,  
J=5.9Hz), 8.95 (1H, d, J=5.2Hz)

APCI-MASS : m/z = 377 (M+H<sup>+</sup>)

Preparation 161

4-[4-(7-Piperidinocarbonylheptyloxy)phenyl]benzoic acid

IR (KBr) : 2933, 2858, 1697, 1677, 1637, 1604, 1429,  
1249 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.2-1.8 (16H, m), 2.26 (2H, t,  
J=7.5Hz), 3.2-3.5 (4H, m), 4.01 (2H, t, J=6.4Hz),  
7.03 (2H, d, J=8.8Hz), 7.67 (2H, d, J=8.8Hz), 7.74  
(2H, d, J=8.4Hz), 7.98 (2H, d, J=8.4Hz)

APCI-MASS : m/z = 424 (M+H<sup>+</sup>)

Preparation 162

6-[4-(4-n-Heptyloxyphenyl)piperazin-1-yl]nicotinic acid

IR (KBr) : 2929, 2854, 1695, 1673, 1606, 1577, 1515,  
1421, 1245 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.86 (3H, t, J=6.7Hz), 1.2-1.5 (8H,  
m), 1.6-1.8 (2H, m), 3.0-3.2 (4H, m), 3.6-3.8 (4H,  
m), 3.87 (2H, t, J=6.5Hz), 6.8-7.2 (5H, m), 7.95

100

(1H, dd, J=8.9 and 2.3Hz), 8.62 (1H, d, J=2.3Hz)  
APCI-MASS : m/z = 398 (M+H<sup>+</sup>)

Preparation 163

5 6-[4-[4-(8-Methoxyoctyloxy)phenyl]piperazin-1-yl]-  
nicotinic acid

IR (KBr) : 2933, 2856, 1697, 1672, 1605, 1511, 1421,  
1245 cm<sup>-1</sup>

10 NMR (DMSO-d<sub>6</sub>, δ) : 1.2-1.8 (12H, m), 3.08 (4H, t,  
J=5.0Hz), 3.20 (3H, s), 3.28 (2H, t, J=6.5Hz), 3.78  
(4H, t, J=4.6Hz), 3.87 (2H, t, J=6.4Hz), 6.8-7.0  
(5H, m), 7.95 (1H, dd, J=9.0 and 2.2Hz), 8.65 (1H,  
d, J=2.2Hz), 12.54 (1H, s)

APCI-MASS : m/z = 442 (M+H<sup>+</sup>)

15

Preparation 164

4-[5-[4-(4-n-Propyloxyphenyl)phenyl]-1,3,4-thiadiazol-2-  
yl]benzoic acid

IR (KBr) : 1685, 1537, 1423, 817 cm<sup>-1</sup>

20 NMR (DMSO-d<sub>6</sub>, δ) : 1.00 (3H, t, J=6.7Hz), 1.6-1.8 (2H,  
m), 4.00 (2H, t, J=6.6Hz), 7.0-7.2 (2H, d,  
J=8.6Hz), 7.6-8.1 (10H, m)

APCI-MASS : m/z = 417 (M+H)<sup>+</sup>

25 Preparation 165

To a solution of Ethyl 4-[5-(4-n-pentyloxyphenyl)-  
isoxazol-3-yl]benzoate (6.33 g) in ethanol (60 ml) and  
tetrahydrofuran (90 ml) was added 2N sodium hydroxide aqueous  
solution (12.5 ml) at 80°C. The mixture was refluxed for 1  
30 hour and poured into ice-water. The suspension was adjusted  
to pH 2.0 with 1N HCl. The precipitate was collected by  
filtration, washed with water and dried to give 4-[5-(4-n-  
pentyloxyphenyl)isoxazol-3-yl]benzoic acid (5.80 g).

35 IR (KBr) : 2939, 2867, 1681, 1614, 1429, 1255, 1178,  
821 cm<sup>-1</sup>

101

08809723, 052197  
267250, E2760880



NMR (DMSO-d<sub>6</sub>, δ) : 0.91 (3H, t, J=7.1Hz), 1.3-1.5 (4H, m), 1.6-1.8 (2H, m), 4.04 (2H, t, J=6.5Hz), 7.11 (2H, d, J=8.9Hz), 7.54 (1H, s), 7.85 (2H, d, J=8.9Hz), 7.98 (2H, d, J=8.6Hz), 8.11 (2H, d, J=8.6Hz)

APCI-MASS : m/z = 352 (M+H)<sup>+</sup>

The following compounds (Preparations 166 to 170) were obtained according to a similar manner to that of Preparation 40.

Preparation 166

5-[4-(4-n-Hexyloxyphenyl)piperazin-1-yl]picolic acid trihydrochloride

IR (KBr) : 1689.3, 1577.5, 1511.9, 1241.9 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.88 (3H, t, J=6.5Hz), 1.15-1.5 (6H, m), 1.6-1.8 (2H, m), 3.1-3.25 (4H, m), 3.45-3.6 (4H, m), 3.89 (2H, t, J=6.4Hz), 6.84 (2H, d, J=9.1Hz), 6.97 (2H, d, J=9.1Hz), 7.43 (1H, dd, J=8.8 and 3.0Hz), 7.90 (1H, dd, J=8.8 and 0.7Hz), 8.41 (1H, dd, J=3.0 and 0.7Hz)

APCI-MASS : m/z = 384 (M<sup>+</sup>+H)

Preparation 167

4-[4-(4-Phenylcyclohexyl)piperazin-1-yl]benzoic acid dihydrochloride

IR (KBr) : 1700.9, 1606.4, 1220.7, 1180.2 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.4-1.85 (4H, m), 1.9-2.05 (2H, m), 2.2-2.4 (2H, m), 3.1-3.5 (6H, m), 3.5-3.7 (2H, m), 3.9-4.2 (2H, m), 7.06 (2H, d, J=8.8Hz), 7.1-7.4 (5H, m), 7.83 (2H, d, J=8.8Hz)

APCI-MASS : m/z = 365 (M<sup>+</sup>+H)

Preparation 168

4-(4-Trans-n-pentylcyclohexyl)benzoic acid

102

08309723-052197

IR (KBr) : 1681.6, 1423.2, 1290.1  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.6\text{Hz}$ ), 1.0-1.6 (13H, m), 1.89 (4H, d,  $J=10\text{Hz}$ ), 2.54 (1H, t,  $J=12\text{Hz}$ ), 7.30 (2H, d,  $J=8.3\text{Hz}$ ), 8.03 (2H, d,  $J=8.3\text{Hz}$ )

5 APCI-MASS :  $m/z = 274$  ( $\text{M}^+ + \text{H}$ )

Preparation 169

4-(4-Piperidinopiperidin-1-yl)benzoic acid

IR (KBr) : 1710.6, 1403.9  $\text{cm}^{-1}$

10 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.6-2.1 (8H, m), 2.17 (2H, d,  $J=12\text{Hz}$ ), 2.7-3.05 (4H, m), 3.2-3.5 (1H, m), 3.35 (2H, d,  $J=12\text{Hz}$ ), 4.05 (2H, d,  $J=13\text{Hz}$ ), 7.01 (2H, d,  $J=8.9\text{Hz}$ ), 7.77 (2H, d,  $J=8.9\text{Hz}$ ), 10.84 (1H, s)

APCI-MASS :  $m/z = 289$  ( $\text{M}^+ + \text{H}$ )

15

Preparation 170

3-Chloro-4-[4-(4-n-hexyloxyphenyl)piperazin-1-yl]benzoic acid dihydrochloride

IR (KBr) : 1712.5, 1598.7, 1513.8, 1251.6  $\text{cm}^{-1}$

20 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.6\text{Hz}$ ), 1.2-1.5 (6H, m), 1.6-1.8 (2H, m), 3.4-3.6 (8H, m), 3.98 (2H, t,  $J=6.4\text{Hz}$ ), 7.02 (2H, d,  $J=9.0\text{Hz}$ ), 7.32 (1H, d,  $J=8.1\text{Hz}$ ), 7.60 (2H, d,  $J=9.0\text{Hz}$ ), 7.89 (1H, d,  $J=8.1\text{Hz}$ ), 8.02 (1H, s)

25 APCI-MASS :  $m/z = 417$  ( $\text{M}^+ + \text{H}$ )

The following compounds (Preparations 171 to 175) were obtained according to a similar manner to that of Preparation 41.

30

Preparation 171

Ethyl [4-(4-octylphenyl)-2,3-dihydro-4H-1,2,4-triazole-3-one-2-yl]acetate

35 IR (KBr) : 2921.6, 1764.5, 1715, 1197.6  $\text{cm}^{-1}$

103

08809723 052197 267250 2260880

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.88 (3H, t, J=6.7Hz), 1.30 (3H, t, J=7.1Hz), 1.2-1.4 (10H, m), 1.5-1.7 (2H, m), 2.63 (2H, t, J=7.9Hz), 4.26 (2H, q, J=7.1Hz), 4.64 (2H, s), 7.28 (2H, d, J=8.4Hz), 7.44 (2H, d, J=8.4Hz), 7.71 (1H, s)

Preparation 172

4-[4-(4-tert-Butoxycarbonylpiperazin-1-yl)phenyl]-2-(4-methylpentyl)-2,3-dihydro-4H-1,2,4-triazol-3-one

IR (KBr) : 1687.4 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.90 (6H, d, J=6.5Hz), 1.1-1.4 (2H, m), 1.49 (9H, s), 1.4-1.9 (3H, m), 3.16 (4H, t, J=4.9Hz), 3.59 (4H, t, J=4.9Hz), 3.82 (2H, t, J=7.3Hz), 6.98 (2H, d, J=9.0Hz), 7.41 (2H, d, J=9.0Hz), 7.61 (1H, s)

Preparation 173

Methyl 6-(8-bromooctyloxy)-2-naphthoate

IR (KBr) : 2933.2, 2856.1, 1720.2, 1294, 1209.1 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.3-1.6 (8H, m), 1.75-2.0 (4H, m), 3.42 (2H, t, J=6.8Hz), 3.96 (3H, s), 4.09 (2H, t, J=6.5Hz), 7.14 (1H, d, J=1.7Hz), 7.19 (1H, dd, J=8.9 and 1.7Hz), 7.73 (1H, d, J=8.7Hz), 7.83 (1H, d, J=8.9Hz), 8.01 (1H, dd, J=8.7 and 1.7Hz), 8.51 (1H, d, J=1.7Hz)

APCI-MASS : m/z = 393 (M<sup>+</sup>+H)

Preparation 174

4-[4-(6-n-Propyloxyhexyloxy)phenyl]benzoic acid

IR (KBr) : 2937, 2858, 1695, 1683, 1604, 1430, 1290, 1247, 1195 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.85 (3H, t, J=7.4Hz), 1.3-1.9 (10H, m), 3.2-3.4 (4H, m), 4.01 (2H, t, J=6.3Hz), 7.04 (2H, d, J=8.7Hz), 7.67 (2H, d, J=8.7Hz), 7.74 (2H, d, J=8.3Hz), 7.98 (2H, d, J=8.3Hz), 12.9 (1H,

104

s)

APCI-MASS :  $m/z = 357$  ( $M+H^+$ )

Preparation 175

5 4-[4-(6-Bromohexyloxy)phenyl]bromobenzene

NMR ( $CDCl_3$ ,  $\delta$ ) : 1.40-1.65 (4H, m), 1.70-2.00 (4H, m),  
3.43 (2H, t,  $J=6.7$ Hz), 4.00 (2H, t,  $J=6.4$ Hz), 6.95  
(2H, d,  $J=8.8$ Hz), 7.30-7.60 (6H, m)

10 The following compounds (Preparations 176 to 180) were  
obtained according to a similar manner to that of Preparation  
43.

Preparation 176

15 4-[4-(4-n-Pentyloxyphenyl)piperazin-1-yl]benzoic acid  
dihydrochloride

IR (KBr) : 1668.1, 1602.6, 1510.0, 1228.4  $cm^{-1}$

20 NMR ( $DMSO-d_6$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.9$ Hz), 1.2-1.5 (5H,  
m), 1.6-1.9 (2H, m), 3.0-3.2 (4H, m), 3.4-3.6 (4H,  
m), 3.88 (2H, t,  $J=6.4$ Hz), 6.83 (2H, d,  $J=9$ Hz),  
6.9-7.1 (4H, m), 7.79 (2H, d,  $J=8.8$ Hz), 12.32 (1H,  
s)

APCI-MASS :  $m/z = 369$  ( $M+H^+$ )

25 Preparation 177

4-[4-(4-n-Heptyloxyphenyl)piperazin-1-yl]benzoic acid  
dihydrochloride

IR (KBr) : 1666.2, 1600.6, 1511.9  $cm^{-1}$

30 NMR ( $CDCl_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.9$ Hz), 1.2-2.0 (10H,  
m), 3.1-3.3 (4H, m), 3.4-3.6 (4H, m), 3.92 (2H, t,  
 $J=6.4$ Hz), 6.8-7.1 (6H, m), 8.00 (2H, d,  $J=8.8$ Hz)

Preparation 178

35 4-[4-[4-(4-Methylpentyloxy)phenyl]piperazin-1-yl]benzoic

105

0809723.052197  
267250. E2260880

acid dihydrochloride

IR (KBr) : 1668.1, 1602.6, 1510.0, 1236.1  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.89 (6H, d,  $J=6.5\text{Hz}$ ), 1.2-1.4 (2H, m), 1.4-1.8 (3H, m), 3.0-3.2 (4H, m), 3.3-3.5 (4H, m), 3.87 (2H, t,  $J=6.3\text{Hz}$ ), 6.83 (2H, d,  $J=9.0\text{Hz}$ ), 6.9-7.1 (4H, m), 7.79 (2H, d,  $J=8.8\text{Hz}$ ), 12.33 (1H, s)

APCI-MASS :  $m/z = 383$  ( $M+H^+$ )

10 Preparation 179

4-[4-[4-(8-Bromooctyloxy)phenyl]piperazin-1-yl]benzoic acid dihydrochloride

IR (KBr) : 1670.1, 1602.6, 1511.9, 1234.2  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.2-1.5 (8H, m), 1.6-1.9 (4H, m), 3.0-3.2 (4H, m), 3.2-3.5 (4H, m), 3.52 (2H, t,  $J=6.7\text{Hz}$ ), 3.88 (2H, t,  $J=6.4\text{Hz}$ ), 6.83 (2H, d,  $J=9.1\text{Hz}$ ), 6.94 (2H, d,  $J=9.1\text{Hz}$ ), 7.02 (2H, d,  $J=8.9\text{Hz}$ ), 7.79 (2H, d,  $J=8.9\text{Hz}$ )

20 Preparation 180

3-Fluoro-4-[4-(4-n-hexyloxyphenyl)piperazin-1-yl]benzoic acid dihydrochloride

IR (KBr) : 1673.9, 1511.9, 1240.0  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.5\text{Hz}$ ), 1.2-1.5 (6H, m), 1.6-1.8 (2H, m), 3.0-3.5 (8H, m), 3.88 (2H, t,  $J=6.4\text{Hz}$ ), 6.7-7.2 (5H, m), 7.4-7.8 (2H, m), 12.82 (1H, s)

APCI-MASS :  $m/z = 401$  ( $M^++H$ )

30 The following compound was obtained according to a similar manner to that of Preparation 46.

Preparation 181

1-(4-Methoxycarbonylphenyl)-3-(4-n-hexyloxyphenyl)-propan-1,3-dione

106

05809723 052197 267250 E2260880

IR (KBr) : 2956, 2927, 2856, 1722, 1511, 1284,  
1108  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.92 (3H, t,  $J=6.4\text{Hz}$ ), 1.2-2.0 (8H,  
m), 3.96 (3H, s), 4.04 (2H, t,  $J=6.5\text{Hz}$ ), 6.82 (1H,  
s), 6.97 (2H, d,  $J=8.7\text{Hz}$ ), 7.9-8.1 (4H, m), 8.14  
(2H, d,  $J=8.3\text{Hz}$ )

APCI-MASS :  $m/z = 383$  ( $\text{M}+\text{H}^+$ )

The following compounds (Preparations 182 to 185) were  
obtained according to a similar manner to that of Preparation  
47.

Preparation 182

Methyl 5-(4-octyloxyphenyl)-1-methylpyrazole-3-  
carboxylate

IR (KBr pelet) : 2923, 1724, 1616, 1513, 1446, 1251,  
1120  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.8\text{Hz}$ ), 1.2-1.5 (10H,  
m), 1.7-1.9 (2H, m), 3.90 (3H, s), 3.98 (2H, t,  
 $J=6.6\text{Hz}$ ), 4.20 (3H, s), 6.92 (2H, d,  $J=8.9\text{Hz}$ ), 7.04  
(1H, s), 7.89 (2H, d,  $J=8.9\text{Hz}$ )

APCI-MASS :  $m/z = 345$  ( $\text{M}+\text{H}^+$ )

Preparation 183

Methyl 4-[5-(4-n-pentyloxyphenyl)pyrazol-3-yl]benzoate

IR (KBr) : 3236, 2952, 2873, 1716, 1616, 1508, 1276,  
1174, 1106  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.94 (3H, t,  $J=7.0\text{Hz}$ ), 1.3-1.5 (4H,  
m), 1.7-1.9 (2H, m), 3.92 (3H, s), 3.96 (2H, t,  
 $J=6.7\text{Hz}$ ), 6.78 (1H, s), 6.88 (2H, d,  $J=8.7\text{Hz}$ ), 7.55  
(2H, d,  $J=8.7\text{Hz}$ ), 7.79 (2H, d,  $J=8.4\text{Hz}$ ), 8.02 (2H,  
d,  $J=8.4\text{Hz}$ )

APCI-MASS :  $m/z = 365$  ( $\text{M}+\text{H}^+$ )

Preparation 184

107

Methyl 5-(4-octyloxyphenyl)isoxazole-3-carboxylate

IR (KBr pelet) : 2950, 2921, 1724, 1614, 1510, 1446,  
1257, 1178, 1143, 1009  $\text{cm}^{-1}$

5 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.8\text{Hz}$ ), 1.2-1.6 (10H,  
m), 1.7-1.9 (2H, m), 4.0-4.1 (5H, m), 6.80 (1H, s),  
6.98 (2H, dd,  $J=6.9$  and  $2.1\text{Hz}$ ), 7.73 (2H, dd,  $J=6.9$   
and  $2.1\text{Hz}$ )

APCI-MASS :  $m/z = 332$  ( $M+H^+$ )

10 Preparation 185

Methyl 4-[3-(4-n-hexyloxyphenyl)pyrazol-5-yl]benzoate

IR (KBr) : 2952, 1716, 1616, 1508, 1276, 1106  $\text{cm}^{-1}$

15 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.91 (3H, t,  $J=6.3\text{Hz}$ ), 1.2-1.6 (6H,  
m), 1.7-1.9 (2H, m), 3.8-4.0 (5H, m), 6.76 (1H, s),  
6.86 (2H, d,  $J=8.8\text{Hz}$ ), 7.54 (2H, d,  $J=8.8\text{Hz}$ ), 7.77  
(2H, d,  $J=8.4\text{Hz}$ ), 8.00 (2H, d,  $J=8.4\text{Hz}$ )

APCI-MASS :  $m/z = 379$  ( $M+H^+$ )

Preparation 186

20 A suspension of 1-(4-n-Pentyloxyphenyl)-3-(4-  
ethoxycarbonylphenyl)-1-buten-3-one (74.43 g) and  
hydroxyamine hydrochloride (28.23 g) and potassium carbonate  
(56.11 g) in ethanol (400 ml) was refluxed for 4 hours. The  
mixture was diluted with ethyl acetate, washed with water  
25 (x 2), brine and dried over magnesium sulfate. The solvents  
were removed under reduced pressure to give crude oxime. To  
a solution of crude oxime in dichloroethane (500 ml) was  
added activated-manganese(IV) oxide (200 g). The reaction  
mixture was refluxed for 2 hours and filtered. The residue  
30 was washed with dichloromethane. The solvents were removed  
under reduced pressure and the residue was triturated with  
acetonitrile. The solid was collected by filtration and  
dried to give ethyl 4-[5-(4-n-Pentyloxyphenyl)isoxazol-3-  
yl]benzoate (21.07 g).

35 IR (KBr) : 2945, 2872, 1717, 1615, 1508, 1280,

108

08309723.052197

1108  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.95 (3H, t,  $J=6.9\text{Hz}$ ), 1.3-1.9 (9H, m), 4.01 (2H, t,  $J=6.5\text{Hz}$ ), 4.41 (2H, q,  $J=7.1\text{Hz}$ ), 6.74 (1H, s), 6.99 (2H, d,  $J=8.8\text{Hz}$ ), 7.76 (2H, d,  $J=8.8\text{Hz}$ ), 7.93 (2H, d,  $J=8.4\text{Hz}$ ), 8.15 (2H, d,  $J=8.4\text{Hz}$ )

APCI-MASS :  $m/z = 380$  ( $\text{M}+\text{H}^+$ )

The following compounds (Preparations 187 to 190) were obtained according to a similar manner to that of Preparation 48.

Preparation 187

Methyl 6-[4-[4-(8-Methoxyoctyloxy)phenyl]piperazin-1-yl]nicotinate

IR (KBr) : 2933, 2858, 1722, 1608, 1513, 1432, 1405, 1278, 1245  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.3-1.9 (12H, m), 3.16 (4H, t,  $J=5.0\text{Hz}$ ), 3.33 (3H, s), 3.36 (2H, t,  $J=6.5\text{Hz}$ ), 3.8-4.0 (9H, m), 6.64 (1H, d,  $J=9.1\text{Hz}$ ), 6.85 (2H, d,  $J=9.2\text{Hz}$ ), 6.93 (2H, d,  $J=9.2\text{Hz}$ ), 8.04 (1H, dd,  $J=9.1$  and  $2.2\text{Hz}$ ), 8.81 (1H, d,  $J=2.2\text{Hz}$ )

APCI-MASS :  $m/z = 456$  ( $\text{M}+\text{H}^+$ )

Preparation 188

4-[4-(5-Methoxypentyloxy)phenyl]bromobenzene

IR (KBr) : 2940, 2856, 1604, 1479, 1286, 1255, 1124  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.5-1.9 (6H, m), 3.34 (3H, s), 3.41 (2H, t,  $J=6.1\text{Hz}$ ), 3.99 (2H, t,  $J=6.4\text{Hz}$ ), 6.95 (2H, d,  $J=8.7\text{Hz}$ ), 7.4-7.6 (6H, m)

APCI-MASS :  $m/z = 349$  ( $\text{M}+\text{H}^+$ )

Preparation 189

Methyl 6-(8-methoxyoctyloxy)-2-naphthoate



NMR (DMSO-d<sub>6</sub>, δ) : 1.2-1.6 (10H, m), 1.7-1.9 (2H, m),  
3.20 (3H, s), 3.29 (2H, t, J=6.4Hz), 3.89 (3H, s),  
4.11 (2H, t, J=6.4Hz), 7.24 (1H, dd, J=9.0 and  
2.4Hz), 7.40 (1H, d, J=2.4Hz), 7.88 (1H, d,  
5 J=8.7Hz), 7.94 (1H, dd, J=8.7 and 1.5Hz), 8.03 (1H,  
d, J=9.0Hz), 8.55 (1H, d, J=1.5Hz)

Preparation 190

4-[4-[4-(8-Methoxyoctyloxy)phenyl]piperazin-1-yl]benzoic  
10 acid dihydrochloride

IR (KBr) : 1668.1, 1602.6, 1511.9, 1236.1 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.2-1.8 (12H, m), 3.05-3.2 (4H, m),  
3.29 (2H, t, J=7.1Hz), 3.33 (3H, s), 3.4-3.55 (4H,  
m), 3.88 (2H, t, J=6.4Hz), 6.82 (2H, d, J=9.0Hz),  
15 6.94 (2H, d, J=9.0Hz), 7.02 (2H, d, J=8.8Hz), 7.79  
(2H, d, J=8.8Hz), 12.31 (1H, s)

The following compounds (Preparations 191 to 254) were  
obtained according to a similar manner to that of Preparation  
20 49.

Preparation 191

1-[4-[4-[4-[2-(4-Methylpentyl)-2,3-dihydro-4H-1,2,4-  
triazol-3-one-4-yl]phenyl]piperazin-1-yl]benzoyl]-  
25 benzotriazole 3-oxide

IR (KBr) : 1766.5, 1693.2, 1600.6, 1519.6 cm<sup>-1</sup>

Preparation 192

1-[4-(4-Octylphenyl)-2,3-dihydro-4H-1,2,4-triazol-3-one-  
30 2-yl-acetyl]benzotriazole 3-oxide

IR (KBr) : 2921.6, 1753.0, 1720.0, 1423.2 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 0.88 (3H, t, J=6.7Hz), 1.2-1.4 (10H,  
m), 1.5-1.8 (2H, m), 2.65 (2H, t, J=7.5Hz), 5.46  
(2H, s), 7.30 (2H, d, J=8.5Hz), 7.48 (2H, d,  
35 J=8.5Hz), 7.62 (1H, t, J=8.3Hz), 7.80 (1H, s), 7.82

(1H, t, J=8.3Hz), 8.05 (1H, d, J=8.3Hz), 8.37 (1H, d, J=8.3Hz)

Preparation 193

1-[4-[4-[4-(7-Methoxyheptyloxy)phenyl]piperazin-1-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 1783.8, 1600.6, 1511.9, 1232.3, 1184.1  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.3-1.9 (10H, m), 3.2-3.3 (4H, m), 3.34 (3H, s), 3.38 (2H, t, J=6.4Hz), 3.5-3.7 (4H, m), 3.92 (2H, t, J=6.5Hz), 6.87 (2H, d, J=9.2Hz), 6.95 (2H, d, J=9.2Hz), 7.00 (2H, d, J=9.0Hz), 7.3-7.6 (3H, m), 8.09 (1H, d, J=8.2Hz), 8.15 (2H, d, J=9.0Hz)

Preparation 194

1-[4-[4-(4-n-Heptyloxyphenyl)piperazin-1-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 1783.8, 1600.6, 1511.9, 1230.4, 1184.1  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t, J=6.3Hz), 1.2-1.6 (8H, m), 1.7-1.9 (2H, m), 3.2-3.3 (4H, m), 3.5-3.7 (4H, m), 3.93 (2H, t, J=6.5Hz), 6.87 (2H, d, J=9.2Hz), 6.95 (2H, d, J=9.2Hz), 7.00 (2H, d, J=9.0Hz), 7.3-7.7 (3H, m), 8.09 (1H, d, J=8.2Hz), 8.15 (2H, d, J=9.0Hz)

Preparation 195

1-[4-[4-[4-(4-Methylpentylloxy)phenyl]piperazin-1-yl]benzoyl]benzotriazole 3-oxide

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.92 (6H, d, J=6.6Hz), 1.2-1.4 (2H, m), 1.5-1.9 (3H, m), 3.1-3.3 (4H, m), 3.5-3.7 (4H, m), 3.92 (2H, t, J=6.6Hz), 6.87 (2H, d, J=9.3Hz), 6.96 (2H, d, J=9.3Hz), 7.01 (2H, d, J=9.0Hz), 7.4-7.6 (3H, m), 8.10 (1H, d, J=8.2Hz), 8.15 (2H, d, J=9.0Hz)

Preparation 196

1-[4-[4-(4-n-Pentyloxyphenyl)piperazin-1-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 1787.7, 1600.6, 1511.9, 1232.3, 1184.1  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.93 (3H, t,  $J=6.9\text{Hz}$ ), 1.3-1.6 (4H, m), 1.7-1.9 (2H, m), 3.1-3.4 (4H, m), 3.5-3.8 (4H, m), 3.93 (2H, t,  $J=6.6\text{Hz}$ ), 6.87 (2H, d,  $J=9.2\text{Hz}$ ), 6.92 (2H, d,  $J=9.2\text{Hz}$ ), 7.01 (2H, d,  $J=9.1\text{Hz}$ ), 7.4-7.6 (3H, m), 8.10 (1H, d,  $J=8.2\text{Hz}$ ), 8.15 (2H, d,  $J=9.1\text{Hz}$ )

Preparation 197

1-[4-[4-[8-(1H-Tetrazol-1-yl)octyloxy]phenyl]benzoyl]benzotriazole 3-oxide

and

1-[4-[4-[8-(2H-tetrazol-2-yl)octyloxy]phenyl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 1778.0, 1602.6, 1189.9, 981.6  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.2-1.6 (8H, m), 1.7-1.9 (2H, m), 1.9-2.2 (2H, m), 4.02 (2H, t,  $J=6.4\text{Hz}$ ), 4.44 and 4.66 (2H, t,  $J=7.1\text{Hz}$ ), 7.02 (2H, d,  $J=8.8\text{Hz}$ ), 7.4-7.6 (3H, m), 7.63 (2H, d,  $J=8.8\text{Hz}$ ), 7.79 (2H, d,  $J=8.6\text{Hz}$ ), 8.12 (1H, d,  $J=8.2\text{Hz}$ ), 8.32 (2H, d,  $J=8.6\text{Hz}$ ), 8.51 and 8.60 (1H, s)

Preparation 198

1-[4-[4-[8-(2,6-Dimethylmorpholin-4-yl)octyloxy]phenyl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 1778.0, 1600.6, 977.7  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.18 (6H, d,  $J=6.3\text{Hz}$ ), 1.2-1.7 (10H, m), 1.7-2.0 (4H, m), 2.4-2.6 (2H, m), 2.9-3.2 (2H, m), 3.7-3.9 (2H, m), 4.01 (2H, t,  $J=6.5\text{Hz}$ ), 7.02 (2H, d,  $J=8.8\text{Hz}$ ), 7.4-7.7 (3H, m), 7.63 (2H, d,

112

J=8.8Hz), 7.79 (2H, d, J=8.5Hz), 8.12 (1H, d,  
J=8.1Hz), 8.32 (2H, d, J=8.5Hz)

Preparation 199

5 1-[6-[4-(4-Octyloxyphenyl)piperazin-1-yl]nicotinoyl]-  
benzotriazole 3-oxide

IR (KBr pelet) : 2922, 2854, 1766, 1602, 1513, 1417,  
1234, 1025, 950, 813  $\text{cm}^{-1}$

10 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t, J=6.8Hz), 1.2-1.5 (10H,  
m), 1.7-1.9 (2H, m), 3.1-3.3 (4H, m), 3.9-4.1 (6H,  
m), 6.75 (1H, d, J=9.2Hz), 6.87 (2H, d, J=9.2Hz),  
6.95 (2H, d, J=9.2Hz), 7.4-7.6 (3H, m), 8.10 (1H,  
d, J=8.1Hz), 8.19 (1H, dd, J=9.2 and 2.4Hz), 9.04  
(1H, d, J=2.4Hz)

15 APCI-MASS :  $m/z = 529$  ( $\text{M}+\text{H}^+$ )

Preparation 200

1-[2-(4-Hexyloxyphenyl)benzoxazol-5-yl-carbonyl]-  
benzotriazole 3-oxide

20 IR (KBr) : 2950, 1774, 1623, 1504, 1265, 1176  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.93 (3H, t, J=6.9Hz), 1.3-1.6 (6H,  
m), 1.8-2.0 (2H, m), 4.07 (2H, t, J=6.5Hz), 7.06  
(2H, d, J=8.9Hz), 7.4-7.6 (3H, m), 7.75 (1H, d,  
J=8.6Hz), 8.13 (1H, d, J=8.2Hz), 8.2-8.4 (3H, m),  
8.67 (1H, d, J=1.6Hz)

25 APCI-MASS :  $m/z = 457$  ( $\text{M}+\text{H}^+$ )

Preparation 201

30 1-[4-[4-(4-n-Butyloxyphenyl)phenyl]benzoyl]-  
benzotriazole 3-oxide

IR (KBr) : 2958, 2871, 1776, 1600, 1398, 1255, 1211,  
1037  $\text{cm}^{-1}$

35 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.00 (3H, t, J=7.2Hz), 1.4-1.9 (4H,  
m), 4.03 (2H, t, J=6.4Hz), 7.01 (2H, d, J=8.3Hz),  
7.4-7.8 (9H, m), 7.87 (2H, d, J=8.1Hz), 8.12 (1H,

113

d, J=8.4Hz), 8.36 (2H, d, J=7.9Hz)  
APCI-MASS : m/z = 464 (M+H)<sup>+</sup>

Preparation 202

5 1-[2-(4-Heptyloxyphenyl)pyridin-5-yl-  
carbonyl]benzotriazole 3-oxide

IR (KBr) : 2944, 2867, 1793, 1770, 1589, 1471, 1321,  
1093 cm<sup>-1</sup>

10 NMR (CDCl<sub>3</sub>, δ) : 0.91 (3H, t, J=6.7Hz), 1.2-1.6 (8H,  
m), 1.7-1.9 (2H, m), 4.05 (2H, t, J=6.5Hz), 7.04  
(2H, d, J=8.0Hz), 7.4-7.6 (3H, m), 7.91 (1H, d,  
J=8.5Hz), 8.1-8.2 (3H, m), 8.51 (1H, dd, J=8.5 and  
2.3Hz), 9.47 (1H, d, J=2.3Hz)

APCI-MASS : m/z = 431 (M+H)<sup>+</sup>

Preparation 203

1-[2-(2-Octyloxy pyridin-5-yl)benzoxazol-5-yl-  
carbonyl]benzotriazole 3-oxide

20 IR (KBr pelet) : 2925, 2854, 1787, 1623, 1479, 1263,  
989 cm<sup>-1</sup>

25 NMR (CDCl<sub>3</sub>, δ) : 0.89 (3H, t, J=6.8Hz), 1.2-1.5 (10H,  
m), 1.8-1.9 (2H, m), 4.42 (2H, t, J=6.7Hz), 6.91  
(1H, d, J=8.7Hz), 6.4-6.6 (3H, m), 7.79 (1H, d,  
J=8.6Hz), 8.13 (1H, d, J=8.2Hz), 8.32 (1H, dd,  
J=8.6 and 1.7Hz), 8.41 (1H, dd, J=8.7 and 2.4Hz),  
8.70 (1H, d, J=1.4Hz), 9.07 (1H, d, J=1.9Hz)

APCI-MASS : m/z = 486 (M+H)<sup>+</sup>

Preparation 204

30 1-[2-[4-(4-Hexylphenyl)phenyl]benzoxazol-5-yl-  
carbonyl]benzotriazole 3-oxide

IR (KBr) : 2927, 2854, 1785, 1621, 1490, 1261, 1166,  
1052 cm<sup>-1</sup>

35 NMR (CDCl<sub>3</sub>, δ) : 0.90 (3H, t, J=6.5Hz), 1.2-1.8 (8H,  
m), 2.68 (2H, t, J=7.9Hz), 7.31 (2H, d, J=8.2Hz),

114

7.4-7.7 (5H, m), 7.79-7.81 (3H, m), 8.13 (1H, d, J=8.3Hz), 8.3-8.4 (3H, m), 8.73 (1H, d, J=1.3Hz)  
APCI-MASS : m/z = 517 (M+H<sup>+</sup>)

5 Preparation 205

1-[2-[4-(4-n-Butyloxyphenyl)phenyl]pyridin-5-yl-carbonyl]benzotriazole 3-oxide

IR (KBr) : 2956, 2933, 2871, 1774, 1650, 1591, 1471, 1251 cm<sup>-1</sup>

10 NMR (CDCl<sub>3</sub>, δ) : 1.00 (3H, t, J=7.2Hz), 1.5-1.9 (4H, m), 4.03 (2H, t, J=6.4Hz), 7.02 (2H, d, J=8.6Hz), 7.4-7.6 (3H, m), 7.54 (2H, d, J=7.3Hz), 7.62 (2H, d, J=8.5Hz), 8.02 (1H, d, J=8.3Hz), 8.13 (1H, d, J=8.2Hz), 8.21 (2H, d, J=7.9Hz), 8.57 (1H, dd, J=8.3 and 2.0Hz), 9.54 (1H, d, J=2.0Hz)

15 APCI-MASS : m/z = 465 (M+H)<sup>+</sup>

Preparation 206

1-[4-[4-(5-Phenoxypropyloxy)phenyl]benzoyl]-benzotriazole 3-oxide

20 IR (KBr) : 2944, 2869, 1770, 1600, 1494, 1249, 1189 cm<sup>-1</sup>

25 NMR (CDCl<sub>3</sub>, δ) : 1.6-1.8 (2H, m), 1.8-2.0 (4H, m), 4.01 (2H, t, J=6.3Hz), 4.07 (2H, t, J=6.2Hz), 6.91 (2H, d, J=8.9Hz), 7.04 (2H, d, J=8.7Hz), 7.3-7.6 (4H, m), 7.63 (2H, d, J=8.6Hz), 7.78 (2H, d, J=8.4Hz), 8.12 (1H, d, J=8.1Hz), 8.32 (2H, d, J=8.4Hz)

30 APCI-MASS : m/z = 494 (M+H)<sup>+</sup>

Preparation 207

1-[4-[5-(4-Hexyloxyphenyl)-1,3,4-oxadiazol-2-yl]benzoyl]benzotriazole 3-oxide

35 IR (KBr) : 2956, 2921, 2856, 1778, 1612, 1496, 1261, 1232, 1025 cm<sup>-1</sup>

115

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.92 (3H, t, J=6.7Hz), 1.3-1.6 (6H, m), 1.8-2.0 (2H, m), 4.05 (2H, t, J=6.5Hz), 7.05 (2H, d, J=8.7Hz), 7.4-7.6 (3H, m), 8.10 (2H, d, J=8.7Hz), 8.13 (1H, d, J=7.4Hz), 8.37 (2H, d, J=8.5Hz), 8.45 (2H, d, J=8.5Hz)

APCI-MASS : m/z = 484 (M+H)<sup>+</sup>

Preparation 208

1-[4-[5-(4-n-Hexyloxyphenyl)-1,3,4-thiadiazol-2-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 2952, 2873, 1774, 1602, 1261, 1230, 1176 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.93 (3H, t, J=6.8Hz), 1.3-2.0 (8H, m), 4.04 (2H, t, J=6.5Hz), 7.02 (2H, d, J=8.7Hz), 7.4-7.7 (3H, m), 7.98 (2H, d, J=8.7Hz), 8.13 (1H, d, J=8.7Hz), 8.25 (2H, d, J=8.3Hz), 8.41 (2H, d, J=8.3Hz)

APCI-MASS : m/z = 500 (M+H)<sup>+</sup>

Preparation 209

1-[5-(4-Octyloxyphenyl)-1-methylpyrazol-3-yl-carbonyl]benzotriazole 3-oxide

IR (KBr pelet) : 2939, 2852, 1776, 1687, 1612, 1448, 1249, 995 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.89 (3H, t, J=6.7Hz), 1.3-1.5 (10H, m), 1.7-1.9 (2H, m), 4.01 (2H, t, J=6.5Hz), 4.25 (3H, s), 6.97 (2H, d, J=6.8Hz), 7.4-7.7 (4H, m), 7.78 (2H, d, J=6.8Hz), 8.14 (1H, d, J=8.0Hz)

APCI-MASS : m/z = 448 (M+H)<sup>+</sup>

Preparation 210

1-[4-[5-(4-n-Pentyloxyphenyl)pyrazol-3-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 3251, 2956, 2869, 1780, 1612, 1506, 1232, 985 cm<sup>-1</sup>

116

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.95 (3H, t, J=6.9Hz), 1.3-1.6 (4H, m), 1.7-2.0 (2H, m), 4.01 (2H, t, J=6.6Hz), 6.90 (1H, s), 6.99 (2H, d, J=8.7Hz), 7.4-7.6 (5H, m), 8.0-8.2 (3H, m), 8.33 (2H, d, J=8.4Hz)

5 APCI-MASS : m/z = 468 (M+H<sup>+</sup>)

Preparation 211

1-[5-[4-(4-n-Butoxyphenyl)phenyl]furan-2-yl-carbonyl]benzotriazole 3-oxide

10 IR (KBr) : 2958, 2871, 1781, 1678, 1603, 1535, 1479, 1265 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.00 (3H, t, J=7.3Hz), 1.4-1.9 (4H, m), 4.02 (2H, t, J=6.4Hz), 6.9-7.1 (3H, m), 7.4-8.2 (11H, m)

15 APCI-MASS : m/z = 351 (Methyl ester)

Preparation 212

1-(3-(S)-Hydroxy-2-benzylhexadecanoyl)benzotriazole 3-oxide

20 IR (Neat) : 2854.1, 1814.7, 1459.8, 742.5 cm<sup>-1</sup>

Preparation 213

1-(3-(R)-Benzyloxycarboxylamino-18-methoxyoctadecanoyl)-benzotriazole 3-oxide

25 IR (KBr) : 1805.0, 1729.8, 1695.1 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 1.1-1.65 (30H, m), 3.20 (3H, s), 3.28 (2H, t, J=6.5Hz), 4.01 (1H, m), 5.06 (2H, s), 7.32 (5H, m), 7.4-7.8 (3H, m), 8.12 (1H, d, J=7Hz)

30 Preparation 214

1-(3-(S)-Hydroxyhexadecanoyl)benzotriazole 3-oxide

IR (KBr) : 1710.6, 1498.4, 1429.0, 771.4 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.88 (3H, t, J=6.4Hz), 1.2-1.7 (24H, m), 2.00 (1H, s), 3.1-3.5 (2H, m), 4.30 (1H, m), 7.59 (1H, t, J=7.8Hz), 7.81 (1H, t, J=7.8Hz), 8.02

117

08809723.052197



(1H, d, J=8.3Hz), 8.42 (1H, d, J=8.3Hz)

Preparation 215

1-(3-Methyl-2-tridecenoyl)benzotriazole 3-oxide

5 IR (KBr) : 2927.4, 1791.5, 1633.4, 1081.9  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t, J=6.3Hz), 1.1-1.7 (20H, m), 2.25 (3H, s), 6.08 (1H, s), 7.3-7.6 (3H, m), 8.06 (1H, d, J=8.2Hz)

10 Preparation 216

1-[4-[4-[4-(8-Methoxyoctyloxy)phenyl]piperazin-1-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 1780.0, 1600.6, 1511.9, 1234.2, 1184.1  $\text{cm}^{-1}$

15 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.3-1.9 (12H, m), 3.24 (4H, t, J=5.0Hz), 3.33 (3H, s), 3.37 (2H, t, J=6.8Hz), 3.62 (4H, t, J=5.0Hz), 3.92 (2H, t, J=6.5Hz), 6.8-7.1 (6H, m), 7.35-7.65 (3H, m), 8.09 (1H, d, J=8.2Hz), 8.15 (2H, d, J=9.0Hz)

20 Preparation 217

1-[3-Fluoro-4-[4-(4-n-hexyloxyphenyl)piperazin-1-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 1778.0  $\text{cm}^{-1}$

25 Preparation 218

1-[3-Chloro-4-[4-(4-n-hexyloxyphenyl)piperazin-1-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 1778.0, 1594.8, 1511.9, 1218.8  $\text{cm}^{-1}$

30 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.91 (3H, t, J=6.5Hz), 1.2-1.6 (6H, m), 1.6-1.9 (2H, m), 3.29 (4H, t, J=3.6Hz), 3.44 (4H, t, J=3.6Hz), 3.93 (2H, t, J=6.5Hz), 6.87 (2H, d, J=9.2Hz), 6.97 (2H, d, J=9.2Hz), 7.19 (1H, d, J=8.6Hz), 7.4-7.7 (3H, m), 8.10 (1H, d, J=6.4Hz), 8.14 (1H, dd, J=8.6 and 2.1Hz), 8.27 (1H, d, J=2.1Hz)

35

118

08809723.052197  
20250723 12:50:23

APCI-MASS :  $m/z = 534 (M^+ + H)$

Preparation 219

1-[4-(4-Piperidinopiperidin-1-yl)benzoyl]benzotriazole  
3-oxide

IR (KBr) : 1758.8, 1602.6, 1186.0  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.35-1.8 (8H, m), 1.96 (2H, d,  $J=13\text{Hz}$ ), 2.45-2.7 (5H, m), 2.97 (2H, td,  $J=12.8$  and  $2.6\text{Hz}$ ), 4.04 (2H, d,  $J=13\text{Hz}$ ), 6.93 (2H, d,  $J=9.2\text{Hz}$ ), 7.35-7.6 (3H, m), 8.1-8.4 (3H, m).

Preparation 220

1-[3-[4-(4-n-Hexyloxyphenyl)piperazin-1-yl]pyridazin-6-yl-carbonyl]benzotriazole 3-oxide

IR (KBr) : 1787.7, 1585.2, 1511.9, 1240.0  $\text{cm}^{-1}$

Preparation 221

1-[5-[4-(4-n-Hexyloxyphenyl)piperazin-1-yl]picolinoyl]-benzotriazole 3-oxide

IR (KBr) : 1766.5, 1575.6, 1511.9, 1232.3  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.91 (3H, t,  $J=6.5\text{Hz}$ ), 1.2-1.6 (6H, m), 1.65-1.9 (2H, m), 3.27 (4H, t,  $J=5.1\text{Hz}$ ), 3.66 (4H, t,  $J=5.1\text{Hz}$ ), 3.93 (2H, t,  $J=6.5\text{Hz}$ ), 6.88 (2H, d,  $J=9.2\text{Hz}$ ), 6.95 (2H, d,  $J=9.2\text{Hz}$ ), 7.25 (1H, dd,  $J=7.6$  and  $2.9\text{Hz}$ ), 7.35-7.6 (3H, m), 8.09 (1H, d,  $J=8.2\text{Hz}$ ), 8.18 (1H, d,  $J=8.9\text{Hz}$ ), 8.52 (1H, d,  $J=2.9\text{Hz}$ )

APCI-MASS :  $m/z = 501 (M^+ + H)$

Preparation 222

1-[4-[4-(4-Cyclohexylphenyl)piperazin-1-yl]benzoyl]-benzotriazole 3-oxide

IR (KBr) : 1770.3, 1602.6, 1515.8, 1232.3, 1186.0  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.15-1.5 (6H, m), 1.65-2.0 (4H, m), 2.45 (1H, m), 3.33 (4H, t,  $J=5.1\text{Hz}$ ), 3.62 (4H, t,

119

J=5.1Hz), 6.92 (2H, d, J=8.7Hz), 6.99 (2H, d, J=9.2Hz), 7.16 (2H, d, J=8.7Hz), 7.35-7.65 (3H, m), 8.09 (1H, d, J=8.2Hz), 8.15 (2H, d, J=9.2Hz)

5 Preparation 223

1-[4-[4-(4-n-Hexylphenyl)piperazin-1-yl]benzoyl]-  
benzotriazole 3-oxide

IR (KBr) : 1768.4, 1602.6, 1515.8, 1230.4, 1184.1  $\text{cm}^{-1}$

10 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t, J=6.5Hz), 1.2-1.45 (6H, m), 1.5-1.7 (2H, m), 2.55 (2H, t, J=7.6Hz), 3.2-3.4 (4H, m), 3.5-3.7 (4H, m), 6.91 (2H, d, J=8.6Hz), 7.00 (2H, d, J=9.1Hz), 7.13 (2H, d, J=8.5Hz), 7.35-7.6 (3H, m), 8.09 (1H, d, J=8.2Hz), 8.15 (2H, d, J=9.1Hz)

15

Preparation 224

1-[4-[4-(4-Phenylcyclohexyl)piperazin-1-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 1780.0, 1762.6, 1602.6, 1234.2, 1182.2  $\text{cm}^{-1}$

20 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.3-1.7 (4H, m), 1.95-2.15 (4H, m), 2.35-2.6 (2H, m), 2.79 (4H, t, J=5.0Hz), 3.49 (4H, t, J=5.0Hz), 6.95 (2H, d, J=9.0Hz), 7.1-7.35 (5H, m), 7.35-7.6 (3H, m), 8.08 (1H, d, J=7.1Hz), 8.12 (2H, d, J=9.0Hz)

25

Preparation 225

1-[4-[4-[1-(4-n-Hexyloxyphenyl)piperidin-4-yl]piperazin-1-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 1768.4, 1602.6, 1511.9, 1234.2  $\text{cm}^{-1}$

30 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t, J=6.5Hz), 1.2-1.55 (6H, m), 1.6-1.9 (4H, m), 1.96 (2H, d, J=11Hz), 2.44 (1H, m), 2.64 (2H, d, J=1.1Hz), 2.77 (4H, t, J=5.0Hz), 3.48 (4H, t, J=5.0Hz), 3.59 (2H, d, J=11Hz), 3.91 (2H, t, J=6.5Hz), 6.7-7.05 (6H, m), 35 7.35-7.6 (3H, m), 8.08 (1H, d, J=6.9Hz), 8.12 (2H,

120

08809723.052197

d,  $J=7.7\text{Hz}$ )

Preparation 226

1-[4-(4-Trans-n-pentylcyclohexyl)benzoyl]benzotriazole  
3-oxide

IR (KBr) : 1799.3, 1778.0, 1608.3, 1228.4, 977.7  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.91 (3H, t,  $J=6.6\text{Hz}$ ), 1.0-1.7 (13H, m), 1.93 (4H, d,  $J=9.8\text{Hz}$ ), 2.62 (1H, t,  $J=12\text{Hz}$ ), 7.35-7.6 (5H, m), 8.09 (1H, d,  $J=7.9\text{Hz}$ ), 8.19 (2H, d,  $J=8.4\text{Hz}$ )

Preparation 227

1-[6-(8-Methoxyoctyloxy)-2-naphthoyl]benzotriazole 3-oxide

IR (KBr) : 2931.3, 2856.1, 1778.0, 1623.8  $\text{cm}^{-1}$

Preparation 228

1-(E)-[3-[4-[4-(7-Fluoroheptyloxy)phenyl]phenyl]-acryloyl]benzotriazole 3-oxide

IR (KBr) : 3070.1, 2935.1, 2859.9, 1700.9, 1619.9, 1596.8  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.30-2.00 (10H, m), 4.02 (2H, t,  $J=6.4\text{Hz}$ ), 4.45 (2H, dt,  $J=47.5$  and  $6.2\text{Hz}$ ), 6.70-8.65 (14H, m)

Preparation 229

1-(6-Heptylnaphthalene-2-carbonyl)benzotriazole 3-oxide

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.75-0.93 (3H, m), 1.10-1.45 (8H, m), 1.55-1.80 (2H, m), 2.68-2.90 (2H, m), 7.35-9.06 (10H, m)

APCI-MASS :  $m/z = 388$  ( $M^++1$ )

Preparation 230

1-(E)-[3-[4-[4-(8-Methoxyoctyloxy)phenyl]phenyl]-acryloyl]benzotriazole 3-oxide

121

05809723 052197

Preparation 231

1-(E)-[3-[4-[4-(5-Hexenyloxy)phenyl]phenyl]acryloyl]-  
benzotriazole 3-oxide

IR (KBr) : 3072.0, 3033.5, 2939.0, 2865.7, 1780.0,  
1693.2, 1619.9, 1596.8  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.43-1.66 (2H, m), 1.66-1.90 (2H,  
m), 2.02-2.23 (2H, m), 3.90-4.16 (2H, m), 4.90-5.13  
(2H, m), 5.72-6.00 (1H, m), 6.93-8.30 (14H, m)

APCI-MASS :  $m/z$  = 337 (Methyl ester,  $M^+ + 1$ )

Preparation 232

1-(E)-[3-[4-[4-(4-Methylpentyloxy)phenyl]phenyl]-  
acryloyl]benzotriazole 3-oxide

IR (KBr) : 3072.0, 3033.5, 2952.5, 2869.6, 1780.0,  
1693.2, 1618.0, 1598.7  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.90 (6H, d,  $J=6.5\text{Hz}$ ), 1.20-1.40  
(2H, m), 1.50-1.90 (3H, m), 3.90-4.10 (2H, m),  
6.40-8.30 (14H, m)

APCI-MASS :  $m/z$  = 442 ( $M^+ + 1$ )

Preparation 233

1-(E)-[3-[4-[4-(6-Fluorohexyloxy)phenyl]phenyl]-  
acryloyl]benzotriazole 3-oxide

IR (KBr) : 3074.0, 3033.5, 2939.0, 2865.7, 1780.0,  
1697.1, 1598.7  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.25-1.83 (6H, m), 4.04 (2H, t,  
 $J=6.5\text{Hz}$ ), 4.45 (2H, dt,  $J=47.5$  and  $6.5\text{Hz}$ ), 6.9-8.3  
(14H, m)

APCI-MASS :  $m/z$  = 460 ( $M^+ + 1$ )

Preparation 234

1-(E)-[3-[4-[4-(6-Methoxyhexyloxy)phenyl]phenyl]-  
acryloyl]benzotriazole 3-oxide

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.30-1.65 (6H, m), 1.65-1.90 (2H,  
m), 3.22 (3H, s), 3.22-3.40 (2H, m), 4.02 (2H, t,

122

J=6.5Hz), 6.5-8.3 (14H, m)

Preparation 235

5 1-[4-[3-(4-n-Hexyloxyphenyl)pyrazol-5-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 2935, 1780, 1610, 1506 1249, 1232, 1178,  
1087  $\text{cm}^{-1}$

10 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.91 (3H, d, J=6.4Hz), 1.2-1.6 (6H, m), 1.7-1.9 (2H, m), 3.98 (2H, t, J=6.5Hz), 6.8-7.0 (3H, m), 7.4-7.6 (5H, m), 8.00 (2H, d, J=8.4Hz), 8.10 (1H, d, J=8.1Hz), 8.28 (1H, d, J=8.4Hz)

APCI-MASS :  $m/z$  = 482 ( $\text{M}+\text{H}^+$ )

Preparation 236

15 1-[4-[4-[4-(6-Methoxyhexyloxy)phenyl]phenyl]benzoyl]-benzotriazole 3-oxide

IR (KBr) : 2935, 2858, 1774, 1600, 1490, 1257,  
1211  $\text{cm}^{-1}$

20 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.4-1.9 (8H, m), 3.35 (3H, s), 3.40 (2H, t, J=6.3Hz), 4.02 (2H, t, J=6.4Hz), 7.00 (2H, d, J=8.7Hz), 7.4-7.8 (7H, m), 7.87 (2H, d, J=8.4Hz), 8.12 (1H, d, J=8.2Hz), 8.36 (2H, d, J=8.4Hz)

APCI-MASS :  $m/z$  = 522 ( $\text{M}+\text{H}^+$ )

Preparation 237

2-[4-[5-[4-(8-Methoxyoctyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 2929, 2854, 1776, 1602, 1469, 1255  $\text{cm}^{-1}$

30 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.2-1.6 (10H, m), 1.7-1.9 (2H, m), 3.33 (3H, s), 3.37 (2H, d, J=6.4Hz), 4.03 (2H, d, J=6.5Hz), 7.00 (2H, d, J=8.9Hz), 7.4-7.6 (3H, m), 7.97 (2H, d, J=8.9Hz), 8.12 (1H, d, J=8.2Hz), 8.23 (2H, d, J=8.7Hz), 8.39 (2H, d, J=8.7Hz)

35 APCI-MASS :  $m/z$  = 558 ( $\text{M}+\text{H}^+$ )

123

08809723.052197  
267250"E260880

Preparation 238

1-[4-(4-n-Butoxyphenyl)cinnamoyl]benzotriazole 3-oxide

IR (KBr) : 2952, 2867, 1778, 1598, 1496, 1249,  
1186  $\text{cm}^{-1}$

5 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.99 (3H, t,  $J=7.3\text{Hz}$ ), 1.55 (2H, tq,  
 $J=7.0$  and  $7.3\text{Hz}$ ), 1.78 (2H, tt,  $J=7.0$  and  $6.4\text{Hz}$ ),  
4.02 (2H, t,  $J=6.4\text{Hz}$ ), 6.75 (1H, d,  $J=16.0\text{Hz}$ ), 7.00  
(2H, d,  $J=8.7\text{Hz}$ ), 7.4-8.2 (9H, m)

APCI-MASS :  $m/z = 414$  ( $\text{M}+\text{H}^+$ )

10

Preparation 239

1-[4-[5-(4-Cyclohexylphenyl)-1,3,4-thiadiazol-2-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 2925, 2850, 1778, 1230, 989  $\text{cm}^{-1}$

15 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.2-1.6 (5H, m), 1.7-2.0 (5H, m),  
2.5-2.7 (1H, m), 7.37 (2H, d,  $J=8.3\text{Hz}$ ), 7.4-7.6  
(3H, m), 7.97 (2H, d,  $J=8.3\text{Hz}$ ), 8.13 (1H, d,  
 $J=8.2\text{Hz}$ ), 8.26 (2H, d,  $J=8.6\text{Hz}$ ), 8.42 (2H, d,  
 $J=8.6\text{Hz}$ )

20 APCI-MASS :  $m/z = 482$  ( $\text{M}+\text{H}^+$ )

Preparation 240

1-[4-[5-[4-(4-n-Propyloxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoyl]benzotriazole 3-oxide

25 IR (KBr) : 1778, 1604, 1488, 1249, 1232, 998  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.07 (3H, t,  $J=7.4\text{Hz}$ ), 1.85 (2H, tq,  
 $J=6.5$  and  $7.4\text{Hz}$ ), 7.02 (2H, d,  $J=8.8\text{Hz}$ ), 7.4-7.7  
(3H, m), 7.61 (2H, d,  $J=8.8\text{Hz}$ ), 7.75 (2H, d,  
 $J=8.5\text{Hz}$ ), 8.14 (1H, d,  $J=8.2\text{Hz}$ ), 8.22 (2H, d,  
30  $J=8.5\text{Hz}$ ), 8.40 (2H, d,  $J=8.8\text{Hz}$ ), 8.48 (2H, d,  
 $J=8.8\text{Hz}$ )

APCI-MASS :  $m/z = 518$  ( $\text{M}+\text{H}^+$ )

Preparation 241

35 1-[4-(5-n-Nonyl-1,3,4-oxadiazol-2-yl)benzoyl]-

124

08809723-052197

benzotriazole 3-oxide

IR (KBr) : 2919, 2850, 1780, 1565, 1415, 1251  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.7\text{Hz}$ ), 1.2-1.6 (12H, m), 1.8-2.0 (2H, m), 2.98 (2H, t,  $J=7.7\text{Hz}$ ), 7.4-7.6 (3H, m), 8.12 (1H, d,  $J=9.0\text{Hz}$ ), 8.28 (2H, d,  $J=8.7\text{Hz}$ ), 8.42 (2H, d,  $J=8.7\text{Hz}$ )

APCI-MASS :  $m/z = 434$  ( $\text{M}+\text{H}^+$ )

Preparation 242

1-[4-[3-(4-n-Hexyloxyphenyl)-1,2,4-oxadiazol-5-yl]-benzoyl]benzotriazole 3-oxide

IR (KBr) : 2946, 2869, 1780, 1251, 1230, 1001  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.92 (3H, t,  $J=6.8\text{Hz}$ ), 1.3-1.6 (6H, m), 1.8-1.9 (2H, m), 4.04 (2H, t,  $J=6.5\text{Hz}$ ), 7.03 (2H, d,  $J=8.9\text{Hz}$ ), 7.4-7.6 (3H, m), 8.0-8.2 (3H, m), 8.46 (4H, s)

APCI-MASS :  $m/z = 484$  ( $\text{M}+\text{H}^+$ )

Preparation 243

1-[4-[5-(4-n-Octyloxyphenyl)-1,3,4-thiadiazol-2-yl]-benzoyl]benzotriazole 3-oxide

IR (KBr) : 2925, 2856, 1774, 1602, 1259, 1232, 989  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.7\text{Hz}$ ), 1.1-1.6 (10H, m), 1.7-1.9 (2H, m), 4.04 (2H, t,  $J=6.5\text{Hz}$ ), 7.01 (2H, d,  $J=8.9\text{Hz}$ ), 7.4-7.6 (3H, m), 7.97 (2H, d,  $J=8.8\text{Hz}$ ), 8.12 (1H, d,  $J=8.2\text{Hz}$ ), 8.24 (2H, d,  $J=8.6\text{Hz}$ ), 8.40 (2H, d,  $J=8.6\text{Hz}$ )

APCI-MASS :  $m/z = 528$  ( $\text{M}+\text{H}^+$ )

Preparation 244

1-[4-[5-(4-Trans-n-pentylcyclohexyl)-1,3,4-thiadiazol-2-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 2952, 2919, 2848, 1785, 1444, 1226, 991  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.9\text{Hz}$ ), 1.0-1.7 (13H, m), 1.94 (2H, d,  $J=12.0\text{Hz}$ ), 2.27 (2H, d,  $J=12.0\text{Hz}$ ),

125



3.19 (1H, tt, J=12.0 and 3.6Hz), 7.4-7.6 (3H, m),  
8.12 (1H, d, J=8.0Hz), 8.19 (2H, d, J=8.6Hz), 8.38  
(2H, d, J=8.6Hz)

APCI-MASS : m/z = 476 (M+H<sup>+</sup>)

5

Preparation 245

1-[4-[3-(4-n-Pentyloxyphenyl)isoxazol-5-  
yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 2948, 2867, 1776, 1610, 1436, 1253, 1002 cm<sup>-1</sup>

10

NMR (CDCl<sub>3</sub>, δ) : 0.95 (3H, t, J=7.1Hz), 1.2-1.6 (4H,  
m), 1.7-1.9 (2H, m), 4.02 (2H, t, J=6.5Hz), 7.0-7.1  
(3H, m), 7.4-7.6 (3H, m), 7.81 (2H, d, J=8.8Hz),  
8.06 (2H, d, J=8.6Hz), 8.12 (1H, d, J=8.0Hz), 8.39  
(2H, d, J=8.6Hz)

15

APCI-MASS : m/z = 469 (M+H<sup>+</sup>)

Preparation 246

1-[4-[5-[4-(8-Methoxyoctyloxy)phenyl]-1,3,4-oxadiazol-2-  
yl]benzoyl]benzotriazole 3-oxide

20

IR (KBr) : 2923, 2854, 1787, 1608, 1494, 1255, 1228,  
993 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 1.2-1.6 (10H, m), 1.7-1.9 (2H, m),  
3.34 (3H, s), 3.38 (2H, t, J=6.4Hz), 4.05 (2H, t,  
J=6.5Hz), 7.04 (2H, d, J=8.8Hz), 7.4-7.6 (3H, s),  
8.1-8.2 (3H, s), 8.36 (2H, d, J=8.7Hz), 8.45 (2H,  
d, J=8.7Hz)

25

APCI-MASS : m/z = 542 (M+H<sup>+</sup>)

Preparation 247

1-[4-[4-(6-Phenylpyridazin-3-yl-oxy)phenyl]benzoyl]-  
benzotriazole 3-oxide

30

IR (KBr) : 1783, 1604, 1423, 1284, 985 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 7.2-8.2 (15H, m), 8.12 (2H, d,  
J=8.3Hz), 8.36 (2H, d, J=8.4Hz)

35

APCI-MASS : m/z = 486 (M<sup>+</sup>+1)

*me*

08809723.052197

Preparation 248

1-[4-[5-(4-n-Octyloxyphenyl)-1,3,4-oxadiazol-2-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 2925, 2854, 1780, 1610, 1496, 1257, 1228,  
1180  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.8\text{Hz}$ ), 1.2-2.0 (12H, m), 4.05 (2H, t,  $J=6.5\text{Hz}$ ), 7.05 (2H, d,  $J=8.7\text{Hz}$ ), 7.4-7.6 (3H, m), 8.0-8.2 (3H, m), 8.37 (2H, d,  $J=8.6\text{Hz}$ ), 8.45 (2H, d,  $J=8.6\text{Hz}$ )

APCI-MASS :  $m/z = 512$  ( $\text{M}+\text{H}^+$ )

Preparation 249

1-[4-[2-(4-n-Hexyloxyphenyl)pyrimidin-6-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 2948, 2861, 1780, 1552, 1413, 1378, 987  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.92 (3H, t,  $J=6.8\text{Hz}$ ), 1.2-1.6 (6H, m), 1.8-2.0 (2H, m), 4.06 (2H, t,  $J=6.5\text{Hz}$ ), 7.04 (2H, d,  $J=9.0\text{Hz}$ ), 7.4-7.6 (3H, m), 7.64 (1H, d,  $J=5.2\text{Hz}$ ), 8.13 (1H, d,  $J=8.2\text{Hz}$ ), 8.44 (4H, s), 8.55 (2H, d,  $J=9.0\text{Hz}$ ), 8.90 (1H, d,  $J=5.2\text{Hz}$ )

APCI-MASS :  $m/z = 494$  ( $\text{M}+\text{H}^+$ )

Preparation 250

1-[4-[4-[8-(2-Ethoxyethoxy)octyloxy]phenyl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 2933, 2861, 1778, 1598, 1247, 1186, 977  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.22 (3H, t,  $J=7.0\text{Hz}$ ), 1.3-2.0 (14H, m), 3.4-3.6 (6H, m), 4.02 (2H, t,  $J=6.5\text{Hz}$ ), 7.02 (2H, d,  $J=8.8\text{Hz}$ ), 7.4-7.6 (3H, m), 7.62 (2H, d,  $J=8.8\text{Hz}$ ), 7.78 (2H, d,  $J=8.6\text{Hz}$ ), 8.10 (1H, d,  $J=8.9\text{Hz}$ ), 8.31 (2H, d,  $J=8.6\text{Hz}$ )

APCI-MASS :  $m/z = 532$  ( $\text{M}+\text{H}^+$ )

Preparation 251

1-[4-[4-[7-(Piperidin-1-yl-carbonyl)heptyloxy]phenyl]-

127

benzoyl]benzotriazole 3-oxide

IR (KBr) : 2935, 2856, 1774, 1631, 1598, 1255,  
1191  $\text{cm}^{-1}$

5 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.3-2.0 (16H, m), 2.37 (2H, t,  
J=7.6Hz), 3.48 (4H, s), 4.02 (2H, t, J=6.4Hz), 7.02  
(2H, d, J=8.6Hz), 7.4-7.6 (3H, m), 7.63 (2H, d,  
J=8.6Hz), 7.78 (2H, d, J=8.3Hz), 8.11 (1H, d,  
J=8.1Hz), 8.31 (2H, d, J=8.3Hz)

10 APCI-MASS :  $m/z$  = 541 ( $\text{M}+\text{H}^+$ )

Preparation 252

1-[6-[4-(4-n-Heptyloxyphenyl)piperazin-1-yl]nicotinoyl]-  
benzotriazole 3-oxide

15 IR (KBr) : 2929, 2856, 1762, 1604, 1510, 1240  $\text{cm}^{-1}$

15 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t, J=6.7Hz), 1.2-1.9 (10H,  
m), 3.20 (4H, t, J=5.0Hz), 3.8-4.0 (6H, m), 6.75  
(1H, d, J=9.5Hz), 6.86 (2H, d, J=9.3Hz), 6.95 (2H,  
d, J=9.3Hz), 7.3-7.6 (3H, m), 8.10 (1H, d,  
J=8.2Hz), 8.19 (1H, dd, J=9.2 and 2.3Hz), 9.05 (1H,  
20 d, J=2.3Hz)

APCI-MASS :  $m/z$  = 515 ( $\text{M}+\text{H}^+$ )

Preparation 253

25 1-[6-[4-[4-(8-Methoxyoctyloxy)phenyl]piperazin-1-  
yl]nicotinoyl]benzotriazole 3-oxide

IR (KBr) : 2929, 2854, 1766, 1602, 1510, 1419,  
1234  $\text{cm}^{-1}$

30 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.3-1.9 (12H, m), 3.2-3.3 (4H, m),  
3.33 (3H, s), 3.36 (2H, t, J=6.4Hz), 3.92 (2H, t,  
J=6.5Hz), 4.0-4.2 (4H, m), 6.75 (1H, d, J=9.1Hz),  
6.87 (2H, d, J=8.9Hz), 7.0-7.2 (2H, m), 7.4-7.6  
(3H, m), 8.09 (1H, d, J=8.1Hz), 8.20 (1H, dd, J=9.1  
and 2.3Hz), 9.05 (1H, d, J=2.3Hz)

35 APCI-MASS :  $m/z$  = 559 ( $\text{M}+\text{H}^+$ )

128

Preparation 254

1-[4-[5-[4-(4-n-Propyloxyphenyl)phenyl]-1,3,4-thiadiazol-2-yl]benzoyl]benzotriazole 3-oxide

IR (KBr) : 1774, 1600, 1234, 985  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.07 (3H, t,  $J=7.3\text{Hz}$ ), 1.85 (2H, tq,  $J=6.5$  and  $7.3\text{Hz}$ ), 3.99 (2H, t,  $J=6.5\text{Hz}$ ), 7.01 (2H, d,  $J=8.7\text{Hz}$ ), 7.4-7.7 (5H, m), 7.72 (2H, d,  $J=8.7\text{Hz}$ ), 8.1-8.2 (2H, m), 8.28 (2H, d,  $J=8.6\text{Hz}$ ), 8.44 (2H, d,  $J=8.6\text{Hz}$ )

APCI-MASS :  $m/z = 534$  ( $M+H$ )<sup>+</sup>

The following compounds (Preparations 255 to 256) were obtained according to a similar manner to that of Preparation 32.

Preparation 255

6-Heptylnaphthalene-2-carboxylic acid

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.6\text{Hz}$ ), 1.15-1.53 (8H, m), 1.58-1.88 (2H, m), 2.80 (2H, t,  $J=7.6\text{Hz}$ ), 7.42 (1H, dd,  $J=1.7$  and  $8.4\text{Hz}$ ), 7.67 (1H, s), 7.84 (1H, d,  $J=8.6\text{Hz}$ ), 7.90 (1H, d,  $J=8.4\text{Hz}$ ), 8.09 (1H, dd,  $J=1.7$  and  $8.6\text{Hz}$ ), 8.68 (1H, s)

APCI-MASS :  $m/z = 271$  ( $M^++1$ ), 285 (methyl ester<sup>+</sup>-1)

Preparation 256

3-(E)-[4-[4-(7-Fluoroheptyloxy)phenyl]phenyl]acrylic acid

IR (KBr) : 3037.3, 2935.1, 2861.8, 1679.7, 1633.4, 1600.6  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.30-1.85 (10H, m), 4.01 (2H, t,  $J=6.4\text{Hz}$ ), 4.44 (2H, dt,  $J=47.6$  and  $6.1\text{Hz}$ ), 6.54 (1H, d,  $J=15.9\text{Hz}$ ), 7.02 (2H, d,  $J=8.7\text{Hz}$ ), 7.53-7.80 (7H, m)

Preparation 257

129

To a solution of 4-methylpentanol (3.0 ml) in pyridine (20 ml) were added in turn with p-toluenesulfonyl chloride (4.6 g) and 4-N,N-dimethylaminopyridine (1.5 g) at ambient temperature. After stirring at ambient temperature, the reaction mixture was taken up into a mixture of ethyl acetate (100 ml) and water (100 ml). The separated organic layer was washed in turn with hydrochloric acid(1N), water, aqueous sodium hydrogencarbonate, and brine, and dried over magnesium sulfate. Evaporation gave 1-p-Toluenesulfonyloxy-4-methylpentane (5.30 g).

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.83 (6H, d,  $J=6.6\text{Hz}$ ), 1.48 (1H, sept,  $J=6.6\text{Hz}$ ), 1.50-1.70 (2H, m), 2.45 (3H, s), 4.00 (2H, t,  $J=6.6\text{Hz}$ ), 7.34 (2H, d,  $J=8.1\text{Hz}$ ), 7.79 (2H, d,  $J=8.1\text{Hz}$ )

APCI-MASS :  $m/z = 257$  ( $M^++1$ )

#### Preparation 258

To a solution of 4-bromo-4'-n-butyloxybiphenyl (3.05 g) in tetrahydrofuran (60 ml) was added 1.55M n-butyllithium in n-hexane (7.74 ml) at  $-60^\circ\text{C}$  over a period of 10 minutes. The solution was stirred at  $-30^\circ\text{C}$  for 1.5 hours and cooled to  $-60^\circ\text{C}$ . To the solution was added triisopropylborate (3.46 ml) over a period of 5 minutes, and the mixture was stirred for 1.5 hours without cooling. To the solution was added 1N hydrochloric acid (20 ml) and the solution was stirred for 30 minutes and extracted with ethyl acetate. The organic layer was separated and washed with water, brine and dried over magnesium sulfate. The solvents were removed under reduced pressure and the residue was triturated with n-hexane. The solid was collected by filtration and dried under reduced pressure to give 4-(4-n-Butyloxyphenyl)phenylboronic acid (2.31 g).

IR (KBr) : 3398, 2956, 2919, 2871, 1604, 1531, 1392,  $1257\text{ cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.94 (3H, t,  $J=7.3\text{Hz}$ ), 1.4-1.8 (4H,

130

m), 4.01 (2H, t, J=6.3Hz), 7.01 (2H, d, J=8.7Hz),  
7.58 (2H, d, J=7.9Hz), 7.62 (2H, d, J=8.7Hz), 7.84  
(2H, d, J=7.9Hz), 8.03 (2H, s)

5 The following compounds (Preparations 259 to 260) were  
obtained according to a similar manner to that of Preparation  
258.

Preparation 259

10 4-[4-(6-Methoxyhexyloxy)phenyl]phenylboronic acid  
IR (KBr) : 3448, 3392, 2937, 2861, 1606, 1529, 1346,  
1288  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.3-1.8 (8H, m), 3.21 (3H, s), 3.31  
(2H, t, J=6.3Hz), 3.99 (2H, t, J=6.4Hz), 7.00 (2H,  
15 d, J=8.7Hz), 7.5-7.7 (4H, m), 7.84 (2H, d,  
J=8.1Hz), 8.03 (2H, s)  
APCI-MASS : m/z = 329 ( $\text{M}+\text{H}^+$ )

Preparation 260

20 4-[4-(5-Methoxypentyloxy)phenyl]phenylboronic acid  
IR (KBr) : 3473, 3369, 3330, 2935, 2863, 1604, 1531,  
1338, 1251  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.4-1.8 (6H, m), 3.22 (3H, s), 3.3-  
3.4 (2H, m), 3.99 (2H, t, J=6.4Hz), 7.00 (2H, d,  
25 J=8.7Hz), 7.58 (2H, d, J=8.0Hz), 7.61 (2H, d,  
J=8.7Hz), 7.84 (2H, d, J=8.0Hz), 8.04 (2H, s)  
APCI-MASS : m/z = 315 ( $\text{M}+\text{H}^+$ )

Preparation 261

30 To a suspension of 4-Methoxycarbonylphenyl boronic acid  
(648 mg) and 4-iodo-1-heptylpyrazole (876 mg) and  $\text{Pd}(\text{PPh}_3)_4$   
(173 mg) in 1,2-dimethoxyethane (10 ml) was added 2M  $\text{Na}_2\text{CO}_3$   
aq. (3.6 ml). The reaction mixture was stirred at 80°C for 2  
hours under  $\text{N}_2$  atmosphere, and poured into ice-water and  
35 extracted with ethyl acetate. The organic layer was washed

131

0809723.052197  
26250.E260880

with brine, and dried over  $\text{MgSO}_4$ . The solvent was removed under pressure. The residue was subjected to column-chromatography on silica gel 60 (Merk) and eluted with n-hexane/ethyl acetate (80:20). The fractions containing the object compound were combined and evaporated under reduced pressure to give 1-heptyl-4-(4-methoxycarbonylphenyl)pyrazole (0.20 g).

IR (KBr pelet) : 2952, 2920, 2848, 1712, 1610, 1288, 1114, 769  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.7\text{Hz}$ ), 1.1-1.4 (8H, m), 1.7-1.9 (2H, m), 3.85 (3H, s), 4.11 (2H, t,  $J=7.0\text{Hz}$ ), 7.72 (2H, d,  $J=8.5\text{Hz}$ ), 7.93 (2H, d,  $J=8.5\text{Hz}$ ), 7.99 (1H, s), 8.34 (1H, s)

APCI-MASS :  $m/z = 301$  ( $\text{M}+\text{H}^+$ )

The following compounds (Preparations 262 to 268) were obtained according to a similar manner to that of Preparation 261.

#### Preparation 262

Ethyl 4-[4-(4-n-butyloxyphenyl)phenyl]benzoate

IR (KBr) : 2958, 2935, 2871, 1714, 1602, 1396, 1280, 1108  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.99 (3H, t,  $J=7.3\text{Hz}$ ), 1.4-2.0 (7H, m), 4.02 (2H, t,  $J=6.4\text{Hz}$ ), 4.40 (2H, q,  $J=7.1\text{Hz}$ ), 6.98 (2H, d,  $J=6.8\text{Hz}$ ), 7.56 (2H, d,  $J=6.8\text{Hz}$ ), 7.66 (4H, s), 7.68 (2H, d,  $J=8.4\text{Hz}$ ), 8.12 (2H, d,  $J=8.4\text{Hz}$ )

APCI-MASS :  $m/z = 375$  ( $\text{M}+\text{H}^+$ )

#### Preparation 263

Methyl 6-(4-heptyloxyphenyl)nicotinate

IR (KBr) : 2954, 2859, 1724, 1597, 1288, 1251, 1116, 783  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.6\text{Hz}$ ), 1.2-1.5 (8H,

132

m), 1.7-1.9 (2H, m), 3.96 (3H, s), 4.03 (2H, t, J=6.5Hz), 7.00 (2H, d, J=8.8Hz), 7.75 (1H, d, J=8.4Hz), 8.02 (1H, d, J=8.8Hz), 8.30 (1H, dd, J=8.4 and 2.2Hz), 9.23 (1H, d, J=2.2Hz)

5 APCI-MASS : m/z = 328 (M+H<sup>+</sup>)

Preparation 264

Methyl 6-[4-(4-n-butyloxyphenyl)phenyl]nicotinate

IR (KBr) : 2956, 2933, 2871, 1724, 1598, 1282,  
10 1118 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 1.00 (3H, t, J=7.3Hz), 1.4-1.9 (4H, m), 3.98 (3H, s), 4.02 (2H, t, J=6.4Hz), 7.00 (2H, d, J=8.8Hz), 7.59 (2H, d, J=8.8Hz), 7.70 (2H, d, J=8.5Hz), 7.86 (1H, d, J=8.8Hz), 8.13 (2H, d, J=8.5Hz),  
15 8.37 (1H, dd, J=8.8 and 1.6Hz), 9.30 (1H, d, J=1.6Hz)

APCI-MASS : m/z = 362 (M+H<sup>+</sup>)

Preparation 265

20 Methyl 5-[4-(4-n-butyloxyphenyl)phenyl]furan 2-carboxylate

IR (KBr) : 2958, 2933, 2873, 1716, 1483, 1303,  
1139 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 0.99 (3H, t, J=7.3Hz), 1.5-1.9 (4H, m), 3.93 (3H, s), 4.01 (2H, t, J=6.4Hz), 6.75 (1H, d, J=3.6Hz), 6.98 (2H, d, J=8.7Hz), 7.26 (1H, d, J=3.6Hz), 7.56 (2H, d, J=8.4Hz), 7.61 (2H, d, J=8.7Hz), 7.83 (2H, d, J=8.4Hz)

25 APCI-MASS : m/z = 351 (M+H)<sup>+</sup>

30

Preparation 266

Ethyl 4-[4-[4-(6-methoxyhexyloxy)phenyl]phenyl]benzoate

IR (KBr) : 2937, 2863, 1712, 1602, 1396, 1278,  
1108 cm<sup>-1</sup>

35 NMR (CDCl<sub>3</sub>, δ) : 1.4-2.0 (11H, m), 3.34 (3H, s), 3.39

133

08809723.052197  
267250.2260880



(2H, t, J=6.4Hz), 4.01 (2H, t, J=6.4Hz), 4.41 (2H, q, J=7.1Hz), 6.98 (2H, d, J=8.7Hz), 7.56 (2H, d, J=8.7Hz), 7.6-7.8 (6H, m), 8.12 (2H, d, J=8.4Hz)  
APCI-MASS : m/z = 433 (M+H<sup>+</sup>)

5

Preparation 267

4-[4-[4-(5-Methoxypentyloxy)phenyl]phenyl]benzoic acid

IR (KBr) : 2939, 2859, 1679, 1587, 1396, 1321, 1292, 1126 cm<sup>-1</sup>

10

NMR (DMSO-d<sub>6</sub>, δ) : 1.3-1.8 (6H, m), 3.21 (3H, s), 3.2-3.4 (2H, m), 4.01 (2H, t, J=6.5Hz), 7.04 (2H, d, J=8.6Hz), 7.66 (2H, d, J=8.6Hz), 7.7-7.9 (6H, m), 8.03 (2H, d, J=8.2Hz)

APCI-MASS : m/z = 391 (M+H<sup>+</sup>)

15

Preparation 268

Methyl 4-[4-[4-(5-methoxypentyloxy)phenyl]phenyl]phenyl acetate

IR (KBr) : 2937, 2863, 1739, 1604, 1492, 1255 cm<sup>-1</sup>

20

NMR (CDCl<sub>3</sub>, δ) : 1.5-2.0 (6H, m), 3.34 (3H, s), 3.42 (2H, t, J=6.3Hz), 3.68 (2H, s), 3.72 (3H, s), 4.02 (2H, t, J=6.4Hz), 6.97 (2H, d, J=8.7Hz), 7.36 (2H, d, J=8.2Hz), 7.5-7.7 (8H, m)

APCI-MASS : m/z = 419 (M+H<sup>+</sup>)

25

Preparation 269

A solution of 3-[2-(4-Hexylphenylamino)ethyl]-2-oxo-oxazolidine hydrochloride (2.131 g) in 25% hydrobromic acid in acetic acid (13.04 ml) was stirred for 96 hours at ambient temperature. The reaction mixture was pulverized with diisopropyl ether. The precipitate was collected by filtration and added to ethanol (15 ml). The solution was refluxed for 5 hours and pulverized with diisopropyl ether. The precipitate was collected by filtration to give 1-(4-n-Hexylphenyl)piperazine dihydrobromide (2.413 g).

30

35

134

08809723.052197

IR (KBr) : 2921.6, 2711.4, 2485.8, 1452.1, 1012.4  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.6\text{Hz}$ ), 1.1-1.4 (6H, m), 1.4-1.6 (2H, m), 2.49 (2H, t,  $J=8.4\text{Hz}$ ), 3.1-3.4 (8H, m), 6.54 (2H, s), 6.90 (2H, d,  $J=8.7\text{Hz}$ ), 7.08 (2H, d,  $J=8.7\text{Hz}$ ), 8.78 (1H, s)  
APCI-MASS :  $m/z = 247$  ( $\text{M}^+ + \text{H}$ )

The following compounds (Preparations 270 to 274) were obtained according to a similar manner to that of Preparation 269.

Preparation 270

4-[4-(4-n-Hexylphenyl)piperazin-1-yl]benzoic acid dihydrobromide

IR (KBr) : 2956.3, 1691.3, 1664.3, 1602.6, 1232.3  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.5\text{Hz}$ ), 1.2-1.4 (10H, m), 1.4-1.6 (2H, m), 2.51 (2H, t,  $J=7.4\text{Hz}$ ), 3.2-3.6 (8H, m), 7.0-7.2 (6H, m), 7.81 (2H, d,  $J=8.8\text{Hz}$ )

APCI-MASS :  $m/z = 367$  ( $\text{M}^+ + \text{H}$ )

Preparation 271

1-(4-Cyclohexylphenyl)piperazine dihydrobromide

IR (KBr) : 2927.4, 1510.0, 1452.1  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.1-1.5 (6H, m), 1.6-1.9 (4H, m), 2.41 (1H, m), 3.1-3.4 (8H, m), 6.91 (2H, d,  $J=8.7\text{Hz}$ ), 7.11 (2H, d,  $J=8.7\text{Hz}$ ), 8.78 (1H, s)  
APCI-MASS :  $m/z = 245$  ( $\text{M}^+ + \text{H}$ )

Preparation 272

4-[4-(4-Cyclohexylphenyl)piperazin-1-yl]benzoic acid dihydrobromide

IR (KBr) : 1668.1, 1602.6, 1230.4, 1189.9  $\text{cm}^{-1}$   
APCI-MASS :  $m/z = 365$  ( $\text{M}^+ + \text{H}$ )

135

Preparation 273

3-Fluoro-4-[4-(4-hydroxyphenyl)piperazin-1-yl]benzoic acid dihydrobromide

IR (KBr) : 1708.6, 1610.3  $\text{cm}^{-1}$

5 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 3.2-3.6 (8H, m), 6.81 (2H, d,  $J=8.6\text{Hz}$ ), 7.0-7.4 (3H, m), 7.4-7.8 (2H, m)

APCI-MASS :  $m/z = 317$  ( $\text{M}^+ + \text{H}$ )

Preparation 274

10 4-[4-(4-Hydroxyphenyl)piperazin-1-yl]benzoic acid dihydrobromide

IR (KBr) : 1670.1, 1604.5, 1226.5, 775.2  $\text{cm}^{-1}$

15 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 3.0-3.2 (4H, m), 3.3-3.5 (4H, m), 6.68 (2H, d,  $J=8.8\text{Hz}$ ), 6.85 (2H, d,  $J=8.8\text{Hz}$ ), 7.02 (2H, d,  $J=8.8\text{Hz}$ ), 7.79 (2H, d,  $J=8.8\text{Hz}$ ), 8.86 (1H, s), 12.29 (1H, s)

APCI-MASS :  $m/z = 299$  ( $\text{M} + \text{H}^+$ )

Preparation 275

20 A mixture of 4-n-hexyloxyaniline (10 g), ethyl acrylate (56.1 ml), glacial acetic acid (19.25 ml), and cuprous chloride (1.02 g) was heated under reflux with stirring under nitrogen for 26 hours. A solution of the cold product in ether was shaken with water and then with aqueous ammonia.

25 The organic layer was taken and dried over magnesium sulfate. The magnesium sulfate was filtered off, and filtrate was evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel and eluted with hexane - ethyl acetate (9:1). The fractions containing the

30 object compound were combined and evaporated under reduced pressure to give Ethyl 3-[N-(2-ethoxycarbonyl)ethyl]-N-(4-hexyloxyphenyl)amino]propionate (15.756 g).

IR (Neat) : 1733.7, 1513.8, 1241.9, 1182.2  $\text{cm}^{-1}$

35 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.5\text{Hz}$ ), 1.2-1.55 (6H, m), 1.24 (6H, t,  $J=7.1\text{Hz}$ ), 1.65-1.85 (2H, m), 2.51

1760

00009723.052197  
261250.E2260880

(4H, t, J=7.2Hz), 3.53 (4H, t, J=7.2Hz), 3.89 (2H, t, J=6.5Hz), 4.12 (4H, q, J=7.1Hz), 6.72 (2H, d, J=9.3Hz), 6.83 (2H, d, J=9.3Hz)

APCI-MASS : m/z = 394 (M<sup>+</sup>+H)

5

Preparation 276

A suspension of methyl 4-formylbenzoate (4.92 g), hydroxylamine hydrochloride (5.21 g) and sodium acetate (6.15 g) in ethanol (50 ml) was refluxed for 2 hours. The mixture was poured into water and extracted with ethyl acetate and the separated organic layer was washed with brine and dried over magnesium sulfate. The solvents were removed under reduced pressure to give 4-methoxycarbonylbenzaldehyde oxime (5.28 g).

15 IR (KBr) : 3291, 1727, 1438, 1284, 1112 cm<sup>-1</sup>  
NMR (CDCl<sub>3</sub>, δ) : 3.93 (3H, s), 7.65 (2H, d, J=8.3Hz), 8.10 (2H, d, J=8.3Hz), 8.18 (1H, s), 8.27 (1H, s)  
APCI-MASS : m/z = 180

20 The following compound was obtained according to a similar manner to that of Preparation 276.

Preparation 277

N-Hydroxy-4-n-hexyloxybenzamidine

25 IR (KBr) : 3446, 3349, 2937, 2865, 1650, 1610, 1519, 1392, 1253 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>, δ) : 0.88 (3H, t, J=6.4Hz), 1.2-1.8 (8H, m), 3.97 (2H, t, J=6.5Hz), 5.70 (2H, s), 6.90 (2H, d, J=8.4Hz), 7.58 (2H, d, J=8.4Hz), 9.43 (1H, s)  
30 APCI-MASS : m/z = 237 (M+H)<sup>+</sup>

Preparation 278

To a solution of 4-methoxycarbonylbenzaldehyde oxime (896 mg) in N,N-dimethylformamide (10 ml) was added 4N-hydrochloride acid in 1,4-dioxane (1.38 ml) and oxone<sup>R</sup> (1.69

137

g). The suspension was stirred at ambient temperature for 16 hours and poured into ice-water. The object compound was extracted with ethyl acetate and the organic layer was washed with brine, dried over magnesium sulfate. The solvents were removed under reduced pressure to give

4-Methoxycarbonylbenzaldehyde oxime chloride (1.05 g).

IR (KBr) : 3390, 1710, 1436, 1405, 1284, 1232, 1116, 1016  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.95 (3H, s), 8.93 (2H, d,  $J=8.3\text{Hz}$ ),

8.10 (2H, d,  $J=8.7\text{Hz}$ ), 8.39 (1H, s)

APCI-MASS :  $m/z = 176$  ( $\text{M-H}^+-\text{HCl}$ )

#### Preparation 279

A solution of Ethyl 4-oxo-1-(4-n-hexyloxyphenyl)piperidine-3-carboxylate (1.437 g) in 20% hydrochloric acid (7.2 ml) was refluxed for 2 hours, cooled, basified with 60% aqueous sodium hydroxide, and extracted with ethyl acetate. The organic layer was taken and dried over magnesium sulfate. The magnesium sulfate was filtered off, and filtrate was evaporated under reduced pressure to give 1-(4-n-Hexyloxyphenyl)-4-piperidone (0.959 g).

IR (Neat) : 2931.3, 1716.3, 1511.9, 1243.9, 825.4  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.5\text{Hz}$ ), 1.2-1.6 (6H, m), 1.65-1.85 (2H, m), 2.57 (4H, t,  $J=6.1\text{Hz}$ ), 3.46 (4H, t,  $J=6.1\text{Hz}$ ), 3.92 (2H, t,  $J=6.5\text{Hz}$ ), 6.85 (2H, d,  $J=9.3\text{Hz}$ ), 6.95 (2H, d,  $J=9.3\text{Hz}$ )

APCI-MASS :  $m/z = 276$  ( $\text{M}^++\text{H}$ )

#### Preparation 280

A solution of 4-[4-(7-Bromoheptyloxy)phenyl]bromobenzene (0.25 g) in a solution of tetra n-butylammonium fluoride (tetrahydrofuran solution, 1M, 2.9 ml) was heated to 50°C for 2 hours. After cooling to ambient temperature, the solution was taken up into a mixture of ethyl acetate (20 ml) and water (20 ml). The separated organic layer was washed with

128

water, brine, and dried over magnesium sulfate. Evaporation gave a residue which was chromatographed on silica gel (30 ml) eluting with a mixture of n-hexane and ethyl acetate (100:0-97:3, V/V). The fractions which contained the objective compound were collected and evaporated a residue which was triturated with n-hexane to give 4-[4-(7-Fluoroheptyloxy)phenyl]bromobenzene (104 mg).

IR (KBr) : 2937.1, 2859.9, 1606.4  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.20-1.90 (10H, m), 3.99 (2H, t,  $J=6.4\text{Hz}$ ), 4.45 (2H, dt,  $J=47.3$  and  $6.1\text{Hz}$ ), 6.95 (2H, d,  $J=6.7\text{Hz}$ ), 7.40 (2H, d,  $J=6.7\text{Hz}$ ), 7.47 (2H, d,  $J=6.7\text{Hz}$ ), 7.52 (2H, d,  $J=6.7\text{Hz}$ )

The following compound was obtained according to a similar manner to that of Preparation 280.

Preparation 281

4-[4-(6-Fluorohexyloxy)phenyl]bromobenzene

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.40-1.95 (8H, m), 4.01 (2H, t,  $J=6.4\text{Hz}$ ), 4.47 (2H, dt,  $J=47.5$  and  $6.0\text{Hz}$ ), 6.95 (2H, d,  $J=8.6\text{Hz}$ ), 7.35-7.59 (6H, m)

Preparation 282

A solution of 4-[4-(8-Bromooctyloxy)phenyl]bromobenzene (3.7 g) in a mixture of sodium methoxide (4.9M in methanol, 17 ml), N,N-dimethylformamide (20 ml) and tetrahydrofuran (8 ml) was heated to  $80^\circ\text{C}$  for 3 hours. The reaction mixture was taken up into a mixture of ethyl acetate (200 ml) and water (100 ml). The separated organic layer was washed in turn with water, brine, dried over magnesium sulfate. Evaporation gave a residue which was subjected to column chromatography (silica gel, 100 ml) eluting with n-hexane to give 4-[4-(8-Methoxyoctyloxy)phenyl]bromobenzene (2.73 g).

IR (KBr) : 2935.1, 2858.0, 1604.5  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.25-1.70 (10H, m), 1.70-1.95 (2H,

139

m), 3.33 (3H, s), 3.37 (2H, t, J=6.5Hz), 3.99 (2H, t, J=6.5Hz), 6.95 (2H, d, J=8.8Hz), 7.35-7.66 (6H, m)

APCI-MASS : m/z = 391 (M<sup>+</sup>)

5

The following compounds (Preparations 283 to 284) were obtained according to a similar manner to that of Preparation 282.

10 Preparation 283

4-[4-(6-Methoxyhexyloxy)phenyl]bromobenzene

NMR (CDCl<sub>3</sub>, δ) : 1.50-1.70 (6H, m), 1.70-1.95 (2H, m), 3.34 (3H, s), 3.40 (2H, t, J=6.2Hz), 3.99 (2H, t, J=6.5Hz), 6.95 (2H, d, J=8.7Hz), 7.30-7.60 (6H, m)

15

APCI-MASS : m/z = 365 (M<sup>+</sup>+2)

Preparation 284

4-[4-(7-Methoxyheptyloxy)phenyl]bromobenzene

IR (KBr) : 2935.1, 2854.1, 1604.5 cm<sup>-1</sup>

20

NMR (CDCl<sub>3</sub>, δ) : 1.25-1.70 (8H, m), 1.70-1.95 (2H, m), 3.33 (3H, s), 3.37 (2H, t, J=6.4Hz), 3.98 (2H, t, J=6.5Hz), 6.95 (2H, d, J=8.8Hz), 7.35-7.56 (6H, m)

APCI-MASS : m/z = 379 (M<sup>+</sup>+2)

25 Preparation 285

N-(4-octylphenyl)-N'-aminoourea, Formamidine acetate

(12.76 g) and N-carbazoyl-4-octylaniline (6.458 g) in N,N-dimethylformamide (19.4 ml) were stirred at 150°C for 6

30

hours. The reaction mixture was pulverized with water. The precipitate was collected by filtration and washed with water to give 4-(4-Octylphenyl)-2,3-dihydro-4H-1,2,4-triazol-3-one (4.27 g).

IR (KBr) : 3214.8, 3085.5, 1704.8 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 0.88 (3H, t, J=6.7Hz), 1.2-1.5 (10H, m), 1.5-1.8 (2H, m), 2.64 (2H, t, J=7.9Hz), 7.29

35

140

08809723.052197

(2H, d, J=8.5Hz), 7.43 (2H, d, J=8.5Hz), 7.67 (1H, d, J=1.3Hz), 10.31 (1H, s)  
APCI-MASS : m/z = 274 (M+H<sup>+</sup>)

5 The following compound (Preparation 286) was obtained according to a similar manner to that of Preparation 285.

Preparation 286

10 4-[4-(4-tert-Butoxycarbonylpiperazin-1-yl)phenyl]-2,3-dihydro-4H-1,2,4-triazol-3-one

IR (KBr) : 3200, 1699.0, 918.0 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 1.49 (9H, s), 3.17 (4H, t, J=4.9Hz), 3.60 (4H, t, J=4.9Hz), 7.00 (2H, d, J=9.0Hz), 7.40 (2H, d, J=9.0Hz), 7.63 (1H, s), 10.4 (1H, s)

15 APCI-MASS : m/z = 346 (M+H<sup>+</sup>)

Preparation 287

20 A mixture of Methyl 6-(1-heptynyl)naphthalene-2-carboxylate (4.51 g) and platinum oxide (0.4 g) in tetrahydrofuran was stirred under 3.5 atm pressure of hydrogen for 5 hours. The catalyst was filtered off and the filtrate was evaporated to give Methyl 6-heptylnaphthalene-2-carboxylate (4.40 g).

25 NMR (CDCl<sub>3</sub>, δ) : 0.88 (3H, t, J=6.6Hz), 1.16-1.50 (8H, m), 1.50-1.80 (2H, m), 2.78 (2H, t, J=7.6Hz), 3.97 (3H, s), 7.39 (1H, dd, J=17 and 8.4Hz), 7.64 (1H, s), 7.79 (1H, d, J=8.6Hz), 7.86 (1H, d, J=8.4Hz), 8.02 (1H, dd, J=1.7 and 8.6Hz), 8.57 (1H, s)

30 APCI-MASS : m/z = 285 (M<sup>+</sup>+1)

The following compound (Preparation 288) was obtained according to a similar manner to that of Preparation 287.

Preparation 288

35 Methyl 6-hexylnaphthalene-2-carboxylate

141

0809723.052197  
261250 E260880



NMR (CDCl<sub>3</sub>, δ) : 0.88 (3H, t, J=6.8Hz), 1.17-1.53 (6H, m), 1.60-1.82 (2H, m), 2.79 (2H, t, J=7.7Hz), 3.97 (3H, s), 7.39 (1H, dd, J=1.7 and 8.4Hz), 7.64 (1H, s), 7.80 (1H, d, J=8.6Hz), 7.86 (1H, d, J=8.4Hz), 8.03 (1H, dd, J=1.7 and 8.6Hz), 8.57 (1H, s)  
APCI-MASS : m/z = 271 (M+1)

Preparation 289

To a stirred solution of Methyl 6-hydroxynaphthalene-2-carboxylate (3.0 g) in dichloromethane (40 ml) were added in turn diisopropylethylamine (3.9 ml) and triflic anhydride (3.0 ml) at -40°C. After stirring at -40°C for 20 minutes, the mixture was taken up into a mixture of ethyl acetate and cold water. The organic layer was separated, washed with brine, dried over magnesium sulfate, and dried in vacuo. The residue was taken up into piperidine (20 ml) and to the solution were added 1-heptyne (4.0 ml) and tetrakis(triphenylphosphine)palladium(0) (0.5 g). After heating to 85°C for 1 hour under nitrogen atmosphere, the reaction mixture was evaporated in vacuo. The residue was diluted with ethyl acetate, and the solution was washed in turn with hydrochloric acid and brine, dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed on silica gel (200 ml) eluting with a mixture of n-hexane and ethyl acetate (9:1, V/V) to give Methyl 6-(1-heptynyl)naphthalene-2-carboxylate (4.01 g).

NMR (CDCl<sub>3</sub>, δ) : 0.94 (3H, t, J=7.1Hz), 1.30-1.70 (6H, m), 2.46 (2H, t, J=7.0Hz), 3.97 (3H, s), 7.50 (1H, dd, J=1.7 and 8.6Hz), 7.80 (1H, d, J=8.6Hz), 7.86 (1H, d, J=8.6Hz), 8.04 (1H, dd, J=1.7 and 8.6Hz), 8.55 (1H, s)

APCI-MASS : m/z = 281 (M<sup>+</sup>+1)

The following compound was obtained according to a similar manner to that of Preparation 289.

142

Preparation 290

Methyl 6-(1-hexynyl)naphthalene-2-carboxylate

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.97 (3H, t, J=7.1Hz), 1.40-1.71 (4H, m), 2.47 (2H, t, J=6.8Hz), 3.98 (3H, s), 7.50 (1H, dd, J=1.5 and 8.5Hz), 7.79 (1H, d, J=8.6Hz), 7.85 (1H, d, J=8.5Hz), 7.92 (1H, s), 8.04 (1H, dd, J=1.7 and 8.6Hz), 8.55 (1H, s)

APCI-MASS : m/z = 267 (M<sup>+</sup>+1)

Preparation 291

To a solution of 4-octylaniline (5 ml) in a mixture of pyridine (12.5 ml) and chloroform (40 ml) was added phenyl chloroformate (2.95 ml) and stirred for 1.5 hours at ambient temperature. The reaction mixture was added to a mixture of water and ethyl acetate. The organic layer was taken and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give 4-Octyl-N-phenoxy carbonylaniline (4.51 g)

IR (KBr) : 3318.9, 1714.4, 1234.2 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.88 (3H, t, J=6.2Hz), 1.2-1.4 (10H, m), 1.5-1.7 (2H, m), 2.57 (2H, t, J=7.3Hz), 6.88 (1H, s), 7.1-7.5 (9H, m)

The following compounds (Preparations 292 to 299) were obtained according to a similar manner to that of Preparation 291.

Preparation 292

4-(4-tert-Butoxycarbonylpiperazin-1-yl)-N-phenoxy carbonylaniline

IR (KBr) : 3309.2, 1743.3, 1658.5, 1197.6 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.48 (9H, s), 3.08 (4H, t, J=5.3Hz), 3.58 (4H, t, J=5.3Hz), 6.87 (1H, s), 6.91 (2H, d, J=9Hz), 7.1-7.5 (7H, m)

APCI-MASS : m/z = 398 (M+H<sup>+</sup>)

143

Preparation 293

1-(4-Cyclohexylbenzoyl)-2-(4-methoxycarbonylbenzoyl)-hydrazine

IR (KBr) : 3236, 2925, 2852, 1726, 1679, 1637, 1278, 1110  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 1.1-1.5 (5H, m), 1.6-2.0 (5H, m), 2.60 (1H, m), 3.90 (3H, s), 7.37 (2H, d,  $J=8.0\text{Hz}$ ), 7.85 (2H, d,  $J=8.0\text{Hz}$ ), 8.0-8.2 (4H, m), 10.48 (1H, s), 10.68 (1H, s)

APCI-MASS :  $m/z = 381$  ( $\text{M}+\text{H}$ )<sup>+</sup>

Preparation 294

1-[4-(Piperidin-1-yl)benzoyl]-2-(4-methoxycarbonylbenzoyl)hydrazine

IR (KBr) : 3500, 3286, 2941, 2854, 1712, 1689, 1650, 1606, 1286, 1242  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 1.59 (6H, s), 3.33 (4H, s), 3.90 (3H, s), 6.97 (2H, d,  $J=8.8\text{Hz}$ ), 7.79 (2H, d,  $J=8.8\text{Hz}$ ), 8.02 (2H, d,  $J=8.4\text{Hz}$ ), 8.09 (2H, d,  $J=8.4\text{Hz}$ ), 10.23 (1H, s), 10.57 (1H, s)

APCI-MASS :  $m/z = 382$  ( $\text{M}+\text{H}$ )<sup>+</sup>

Preparation 295

1-[4-(4-n-Propyloxyphenyl)benzoyl]-2-(4-methoxycarbonylbenzoyl)hydrazine

IR (KBr) : 3230, 1724, 1679, 1654, 1280, 1108  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 1.00 (3H, d,  $J=7.5\text{Hz}$ ), 1.76 (2H, tq,  $J=6.5$  and  $7.5\text{Hz}$ ), 3.91 (3H, s), 7.05 (2H, d,  $J=8.7\text{Hz}$ ), 7.71 (2H, d,  $J=8.7\text{Hz}$ ), 7.79 (2H, d,  $J=8.5\text{Hz}$ ), 8.00 (2H, d,  $J=8.5\text{Hz}$ ), 8.05 (2H, d,  $J=8.6\text{Hz}$ ), 8.11 (2H, d,  $J=8.6\text{Hz}$ ), 10.60 (1H, s), 10.72 (1H, s)

APCI-MASS :  $m/z = 433$  ( $\text{M}+\text{H}$ )<sup>+</sup>

Preparation 296

144

1-(4-Methoxycarbonylbenzoyl)-2-decanoylhydrazine

IR (KBr) : 3220, 2919, 2850, 1724, 1643, 1600, 1567,  
1479, 1284  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.8\text{Hz}$ ), 1.2-1.7  
(14H, m), 2.18 (2H, t,  $J=7.4\text{Hz}$ ), 3.89 (3H, s), 7.97  
(2H, d,  $J=8.5\text{Hz}$ ), 8.06 (2H, d,  $J=8.5\text{Hz}$ ), 9.15 (1H,  
s), 10.49 (1H, s)

APCI-MASS :  $m/z = 349$  ( $\text{M}+\text{H}^+$ )

Preparation 297

1-(4-Methoxycarbonylbenzoyl)-2-(trans-4-n-  
pentylcyclohexylcarbonyl)hydrazine

IR (KBr) : 3201, 2923, 2852, 1727, 1600, 1567, 1479,  
1282  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.9\text{Hz}$ ), 0.9-1.0 (2H,  
m), 1.1-1.5 (11H, m), 1.7-1.9 (4H, m), 2.20 (1H,  
m), 3.88 (3H, s), 7.97 (2H, d,  $J=8.6\text{Hz}$ ), 8.06 (2H,  
d,  $J=8.6\text{Hz}$ ), 9.85 (1H, s), 10.46 (1H, s)

APCI-MASS :  $m/z = 375$  ( $\text{M}+\text{H}^+$ )

Preparation 298

1-[4-(8-Methoxyoctyloxy)benzoyl]-2-(4-  
methoxycarbonylbenzoyl)hydrazine

IR (KBr) : 3213, 2935, 2856, 1718, 1600, 1567, 1465,  
1282  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 1.2-1.8 (12H, m), 3.21 (3H, s),  
3.29 (2H, t,  $J=6.4\text{Hz}$ ), 3.90 (3H, s), 4.04 (2H, t,  
 $J=6.5\text{Hz}$ ), 7.04 (2H, d,  $J=8.8\text{Hz}$ ), 7.90 (2H, d,  
 $J=8.8\text{Hz}$ ), 8.04 (2H, d,  $J=8.7\text{Hz}$ ), 8.10 (2H, d,  
 $J=8.7\text{Hz}$ ), 10.41 (1H, s), 10.64 (1H, s)

APCI-MASS :  $m/z = 457$  ( $\text{M}+\text{H}^+$ )

Preparation 299

1-(4-Octyloxybenzoyl)-2-(4-methoxycarbonylbenzoyl)-  
hydrazine

145

IR (KBr) : 3224, 2923, 2854, 1724, 1681, 1643, 1502,  
1434, 1282, 1253, 1106  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.8\text{Hz}$ ), 1.2-1.5  
(10H, m), 1.6-1.8 (2H, m), 3.89 (3H, s), 4.04 (2H,  
5 t,  $J=6.3\text{Hz}$ ), 7.04 (2H, d,  $J=8.7\text{Hz}$ ), 7.90 (2H, d,  
 $J=8.7\text{Hz}$ ), 8.03 (2H, d,  $J=8.6\text{Hz}$ ), 8.10 (2H, d,  
 $J=8.6\text{Hz}$ ), 10.42 (1H, s), 10.64 (1H, s)

APCI-MASS :  $m/z = 427$  ( $\text{M}+\text{H}^+$ )

10 Preparation 300

A solution of Methyl 4-n-hexyloxybenzoate (2.00 g) and  
hydrazine hydrate (4.24 g) in ethanol (10 ml) was refluxed  
for 6 hours. After cooling, the reaction mixture was poured  
into water. The precipitate was collected by filtration,  
15 washed with water and dried over  $\text{P}_2\text{O}_5$  under reduced pressure  
to give N-(4-n-hexyloxybenzoyl)hydrazine (1.96 g).

IR (KBr) : 3311, 2954, 2869, 1623, 1253  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.8\text{Hz}$ ), 1.2-1.5 (6H,  
m), 1.6-1.8 (2H, m), 4.00 (2H, t,  $J=6.5\text{Hz}$ ), 4.40  
20 (2H, s), 6.95 (2H, d,  $J=8.6\text{Hz}$ ), 7.77 (2H, d,  
 $J=8.6\text{Hz}$ ), 9.59 (1H, s)

APCI-MASS :  $m/z = 237$  ( $\text{M}+\text{H}^+$ )

The following compounds (Preparations 301 to 308) were  
25 obtained according to a similar manner to that of Preparation  
300.

Preparation 301

N-(4-Octylphenyl)-N'-aminourea

30 IR (KBr) : 3309.2, 1683.6, 1554.3  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.7\text{Hz}$ ), 1.1-1.4  
(10H, m), 1.4-1.6 (2H, m), 2.48 (2H, t,  $J=8.9\text{Hz}$ ),  
4.32 (2H, s), 7.03 (2H, d,  $J=8.4\text{Hz}$ ), 7.32 (1H, s),  
7.38 (2H, d,  $J=8.4\text{Hz}$ ), 8.50 (1H, s)

Preparation 302

N-[4-(4-tert-Butoxycarbonylpiperazin-1-yl)phenyl]-N'-aminourea

IR (KBr) : 3237.9, 1695.1, 1670.1, 1540.8, 1230.4  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.42 (9H, s), 2.97 (4H, t, J=4.9Hz), 3.44 (4H, t, J=4.9Hz), 4.30 (2H, s), 6.85 (2H, d, J=9.0Hz), 7.26 (1H, s), 7.36 (2H, d, J=9.0Hz), 8.41 (1H, s)

Preparation 303

4-Cyclohexylbenzoylhydrazine

IR (KBr) : 3318, 2925, 2852, 1625, 1606, 1527, 1326  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.1-1.5 (5H, m), 1.6-2.0 (5H, m), 2.4-2.6 (1H, m), 4.44 (2H, s), 7.27 (2H, d, J=8.2Hz), 7.73 (2H, d, J=8.2Hz), 9.66 (1H, s)

APCI-MASS :  $m/z = 219$  (M+H)<sup>+</sup>

Preparation 304

4-(Piperidin-1-yl)benzoylhydrazine

IR (KBr) : 3263, 2852, 1612, 1504, 1245, 1124  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.57 (6H, s), 3.25 (4H, s), 4.35 (2H, s), 6.90 (2H, d, J=9.0Hz), 7.68 (2H, d, J=9.0Hz), 9.44 (1H, s)

APCI-MASS :  $m/z = 220$  (M+H)<sup>+</sup>

Preparation 305

4-(4-n-Propyloxyphenyl)benzoylhydrazine

IR (KBr) : 3350, 3276, 1610, 1494, 1288, 978  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_3$ ,  $\delta$ ) : 0.99 (3H, t, J=7.5Hz), 1.75 (2H, tq, J=6.5 and 7.5Hz), 3.98 (2H, t, J=6.5Hz), 4.50 (2H, s), 7.03 (2H, d, J=8.8Hz), 7.65 (2H, d, J=8.8Hz), 7.69 (2H, d, J=8.4Hz), 7.88 (2H, d, J=8.4Hz), 9.79 (1H, s)

APCI-MASS :  $m/z = 271$  (M+H)<sup>+</sup>

147

Preparation 306

4-Methoxycarbonylbenzoylhydrazine

IR (KBr) : 3322, 3250, 3018, 1727, 1658, 1621, 1565,  
1432, 1280, 1110  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 3.87 (3H, s), 4.58 (2H, s), 7.93  
(2H, dd,  $J=8.6$  and  $3.1\text{Hz}$ ), 7.02 (2H, dd,  $J=8.6$  and  
 $3.1\text{Hz}$ ), 9.97 (1H, s)

APCI-MASS :  $m/z = 195$  ( $\text{M}+\text{H}^+$ )

Preparation 307

Trans-4-n-pentylcyclohexylcarbonylhydrazine

IR (KBr) : 3303, 3199, 2954, 2925, 2850, 1639, 1619,  
1533, 1457  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.8-1.0 (6H, m), 1.1-1.5 (10H, m),  
1.6-2.2 (5H, m), 4.10 (2H, s), 8.85 (1H, s)

APCI-MASS :  $m/z = 213$  ( $\text{M}+\text{H}^+$ )

Preparation 308

4-(8-Methoxyoctyloxy)benzoylhydrazine

IR (KBr) : 3309, 2937, 2852, 1606, 1494, 1253  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 1.2-1.8 (12H, m), 3.20 (3H, s),  
3.25 (2H, t,  $J=6.5\text{Hz}$ ), 3.99 (2H, t,  $J=6.5\text{Hz}$ ), 4.39  
(2H, s), 6.95 (2H, d,  $J=8.8\text{Hz}$ ), 7.77 (2H, d,  
 $J=8.8\text{Hz}$ ), 9.58 (1H, s)

APCI-MASS :  $m/z = 295$  ( $\text{M}+\text{H}^+$ )

Preparation 309

To a stirred solution of 4-bromo-4'-n-heptylbiphenyl  
(2.71 g) in tetrahydrofuran (100 ml) was added dropwise a  
solution of n-butyllithium in a mixture of diethyl ether and  
n-hexane (1.6M, 5.1 ml) at  $-78^\circ\text{C}$ . After stirring at  $-78^\circ\text{C}$   
for 30 minutes, the resultant mixture was added to a solution  
of diethyl oxalate (3.4 ml) in tetrahydrofuran (50 ml) at  
 $-78^\circ\text{C}$ . The resultant mixture was allowed to warm to  $0^\circ\text{C}$  for  
about 1 hour, and to the mixture was added acetic acid (0.5

ml). Evaporation gave a residue which was taken up into a mixture of water and ethyl acetate. The organic layer was separated, washed with brine, dried over magnesium sulfate. Evaporation gave a residue which was chromatographed on silica gel (200 ml) eluting with a mixture of n-hexane and ethyl acetate (10:0-95:5, V/V) to give 1-Ethyl-2-(4-n heptylphenyl)ethanedione (2.23 g).

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.6\text{Hz}$ ), 1.10-1.50 (8H, m), 1.44 (3H, t,  $J=7.1\text{Hz}$ ), 1.50-1.80 (2H, m), 2.66 (2H, t,  $J=7.7\text{Hz}$ ), 4.47 (2H, q,  $J=7.1\text{Hz}$ ), 7.20-7.40 (2H, m), 7.50-7.64 (2H, m), 7.64-7.85 (2H, m), 8.00-8.20 (2H, m)

APCI-MASS :  $m/z = 353$  ( $M^+ + 1$ )

#### Preparation 310

To a suspension of sodium hydride (60% in oil, 0.37 g) in tetrahydrofuran (40 ml) was added by portions 4-acetyl-4'-n-heptylbiphenyl (2.50 g) at ambient temperature. After stirring at ambient temperature for 1 hour, to the solution was added triethyl phosphonoacetate (1.9 ml) and the mixture was heated to reflux for 5 hours. After cooling to ambient temperature, to the mixture was added acetic acid (0.53 ml) and evaporated. The residue was taken up into a mixture of water and ethyl acetate. The separated organic layer was washed with brine, dried over magnesium sulfate and evaporated. The residue was chromatographed on silica gel (200 ml) eluting with mixture of n-hexane and diisopropyl ether (99:1-20:1, V/V) to give Ethyl (E)-3-[4-(4-heptylphenyl)phenyl]-2-butenate (2.19 g).

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.6\text{Hz}$ ), 1.13-1.48 (8H, m), 1.48-1.78 (2H, m), 2.61 (3H, s), 2.65 (2H, t,  $J=7.4\text{Hz}$ ), 4.22 (2H, q,  $J=7.1\text{Hz}$ ), 6.20 (1H, t,  $J=2.7\text{Hz}$ ), 7.23-7.28 (2H, m), 7.50-7.63 (6H, m)

APCI-MASS :  $m/z = 365$  ( $M^+ + 1$ )



Preparation 311

To a solution of 4-bromo-4'-n-heptylbiphenyl (5.1 g) in tetrahydrofuran (60 ml) was added a solution of n-butyllithium in a mixture of n-hexane and diethyl ether (1.6M, 9.7 ml) at -60°C. After stirring at -60°C for 30 minutes, to the mixture was added N,N-dimethylacetamide (4.3 ml) and the reaction mixture was allowed to warm to 0°C. The reaction mixture was taken up into a mixture of cold water and ethyl acetate, and the pH was adjusted to around 1 with 1N hydrochloric acid. The organic layer was separated, washed with brine, dried over magnesium sulfate and evaporated. The residue was chromatographed on silica gel (150 ml) eluting with a mixture of n-hexane and ethyl acetate (20:1, V/V) to give 4-Acetyl-4'-n-heptylbiphenyl (1.60 g).

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.89 (3H, t, J=6.6Hz), 1.05-1.48 (8H, m), 1.48-1.75 (2H, m), 2.65 (2H, t, J=7.6Hz), 2.63 (3H, s), 7.20-7.31 (2H, m), 7.52-7.58 (2H, m), 7.65-7.70 (2H, m), 7.97-8.05 (2H, m)

APCI-MASS : m/z = 295 (M+1)

Preparation 312

To a solution of Methyl 4-[4-(8-hydroxyoctyloxy)phenyl]-benzoate (500 mg) and dihydropyran (141 mg) in dichloromethane (15 ml) was added p-toluenesulfonic acid (5 ml). The mixture was stirred at ambient temperature for 10 minutes and diluted with dichloromethane and washed with water and brine. The separated organic layer was dried over magnesium sulfate and evaporated under reduced pressure to give Methyl 4-[4-(8-tetrahydropyran-2-yl-oxyoctyloxy)phenyl]-benzoate (616 mg).

IR (KBr) : 2935, 2856, 1722, 1602, 1438, 1290, 1199 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.3-2.0 (18H, m), 3.3-3.9 (4H, m), 3.93 (3H, s), 4.00 (2H, t, J=6.5Hz), 4.5-4.6 (1H, m), 6.98 (2H, d, J=8.7Hz), 7.56 (2H, d, J=8.7Hz),

140

7.62 (2H, d, J=8.3Hz), 8.07 (2H, d, J=8.3Hz)

Preparation 313

To a solution of titanium(IV) chloride (11.6 g) in dichloromethane (100 ml) was added 4-n-Pentyloxyacetophenone (10.3 g) and Methyl 4-formylbenzoate (8.21 g) in dichloromethane (50 ml) dropwise at 0°C. To the mixture was added triethylamine (11.15 ml) in dichloromethane (30 ml). The mixture was stirred at 0°C for 30 minutes and diluted with n-hexane. The organic layer was washed with water (four times), brine and dried over magnesium sulfate. The solvents were removed under reduced pressure and the residue was triturated with iso-propyl ether. The solid was collected by filtration and dried to give 1-(4-Methoxycarbonylphenyl)-3-(4-n-pentyloxyphenyl)-1-propen-3-one (4.02 g).

IR (KBr) : 2950, 2910, 2863, 1718, 1654, 1606, 1274, 1176  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.94 (3H, t, J=6.9Hz), 1.3-1.6 (4H, m), 1.8-2.0 (2H, m), 3.93 (3H, s), 4.04 (2H, t, J=6.5Hz), 6.97 (2H, d, J=8.8Hz), 7.60 (1H, d, J=15.7Hz), 7.68 (2H, d, J=8.4Hz), 7.80 (1H, d, J=15.7Hz), 8.0-8.2 (4H, m)

APCI-MASS :  $m/z = 353$  ( $\text{M}+\text{H}^+$ )

Preparation 314

To a solution of titanium(IV) chloride (13.88 g) in dichloromethane (100 ml) was added Ethyl 4-acetylbenzoate (11.53 g) and 4-n-pentyloxybenzaldehyde (12.69 g) in dichloromethane (50 ml) was added dropwise at 0°C. To the mixture was added triethylamine (12.44 ml) in dichloromethane (30 ml). The mixture was stirred at 0°C for 30 minutes and diluted with ethyl acetate. The organic layer was washed with water (four times) and brine and dried over magnesium sulfate. The solvents were removed under reduced pressure and the residue was triturated with n-hexane. The solid was

151

08809723 052197

collected by filtration and dried to give 1-(4-n-Pentyloxyphenyl)-3-(4-ethoxycarbonylphenyl)-1-propen-3-one (13.45 g).

IR (KBr) : 2956, 2929, 2861, 1718, 1656, 1594, 1510, 1272  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.94 (3H, t,  $J=7.1\text{Hz}$ ), 1.3-1.9 (9H, m), 4.01 (2H, t,  $J=6.5\text{Hz}$ ), 4.42 (2H, q,  $J=7.1\text{Hz}$ ), 6.93 (1H, d,  $J=8.7\text{Hz}$ ), 7.37 (1H, d,  $J=15.6\text{Hz}$ ), 7.60 (2H, d,  $J=8.7\text{Hz}$ ), 7.81 (1H, d,  $J=15.6\text{Hz}$ ), 8.03 (2H, d,  $J=8.5\text{Hz}$ ), 8.16 (2H, d,  $J=8.5\text{Hz}$ )

APCI-MASS :  $m/z = 367$  ( $M+H^+$ )

The following compound was obtained according to a similar manner to that of Preparation 314.

#### Preparation 315

Ethyl 4-oxo-1-(4-n-hexyloxyphenyl)piperidine-3-carboxylate

IR (Neat) : 1664.3, 1511.9, 1243.9, 1216.9  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.5\text{Hz}$ ), 1.2-1.5 (6H, m), 1.32 (3H, t,  $J=7.1\text{Hz}$ ), 1.65-1.85 (2H, m), 2.51 (2H, t,  $J=5.8\text{Hz}$ ), 3.31 (2H, t,  $J=5.8\text{Hz}$ ), 3.76 (2H, s), 3.91 (2H, t,  $J=6.5\text{Hz}$ ), 4.26 (2H, q,  $J=7.1\text{Hz}$ ), 6.84 (2H, d,  $J=9.2\text{Hz}$ ), 6.94 (2H, d,  $J=9.2\text{Hz}$ ), 12.06 (1H, s)

APCI-MASS :  $m/z = 348$  ( $M^+ + H$ )

#### Preparation 316

To a solution of 4-n-Hexyloxybenzoylhydrazine (1.96 g) and pyridine (0.74 ml) in tetrahydrofuran (20 ml) was added a solution of terephthalic acid monomethyl ester chloride (1.56 g) in tetrahydrofuran (15 ml) dropwise at  $0^\circ\text{C}$ . The reaction mixture was stirred at room temperature for 2 hours, and poured into water. The precipitate was collected by filtration and washed with acetonitrile. The residue was

152

dried under reduced pressure to give 1-(4-n-Hexyloxybenzoyl)-  
2-(4-methoxycarbonylbenzoyl)hydrazine (2.99 g).

IR (KBr) : 3230, 3023, 2954, 2858, 1724, 1681, 1643,  
1280, 1251, 1105  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.6\text{Hz}$ ), 1.2-1.5 (6H,  
m), 1.6-1.8 (2H, m), 3.90 (3H, s), 4.04 (2H, t,  
 $J=6.4\text{Hz}$ ), 7.04 (2H, d,  $J=8.7\text{Hz}$ ), 7.90 (2H, d,  
 $J=8.7\text{Hz}$ ), 8.03 (2H, d,  $J=8.4\text{Hz}$ ), 8.10 (2H, d,  
 $J=8.4\text{Hz}$ ), 10.42 (1H, s), 10.65 (1H, s)

APCI-MASS :  $m/z = 399 (M+H)^+$

#### Preparation 317

A mixture of 1-(4-n-Hexyloxyphenyl)-4-piperidone (0.823  
g), 1-(4-Ethoxycarbonylphenyl)piperazine (0.7 g), and  
titanium(IV) isopropoxide (1.11 ml) was stirred at room  
temperature. After 1 hour, the IR spectrum of the mixture  
showed no ketone band, and the viscous solution was diluted  
with absolute ethanol (3 ml). Sodium cyanoborohydride (0.121  
g) was added, and the solution was stirred for 3 hours.  
Water (3 ml) was added with stirring, and the resulting in  
organic precipitate was filtered and washed with ethanol.  
The filtrate was extracted with ethyl acetate. The organic  
layer was taken and dried over magnesium sulfate. The  
magnesium sulfate was filtered off, and filtrate was  
evaporated under reduced pressure to give Ethyl 4-[4-[1-(4-n-  
hexyloxyphenyl)piperidin-4-yl]piperazin-1-yl]benzoate (331  
mg).

IR (KBr) : 1708.6, 1606.4, 1511.9, 1284.4, 1236.1  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.5\text{Hz}$ ), 1.2-1.55 (6H,  
m), 1.37 (3H, t,  $J=7.1\text{Hz}$ ), 1.6-1.85 (4H, m), 1.95  
(2H, d,  $J=12\text{Hz}$ ), 2.41 (1H, m), 2.62 (2H, d,  
 $J=11\text{Hz}$ ), 2.75 (4H, t,  $J=5.0\text{Hz}$ ), 3.35 (4H, t,  
 $J=5.0\text{Hz}$ ), 3.58 (2H, d,  $J=11\text{Hz}$ ), 3.90 (2H, t,  
 $J=6.5\text{Hz}$ ), 4.32 (2H, q,  $J=7.1\text{Hz}$ ), 6.7-7.0 (6H, m),  
7.92 (2H, d,  $J=9.0\text{Hz}$ )

153

APCI-MASS :  $m/z = 494 (M^+ + H)$

The following compound was obtained according to a similar manner to that of Preparation 317.

Preparation 318

1-tert-Butoxycarbonyl-4-(4-phenylcyclohexyl)piperazine

IR (KBr) : 1697.1, 1245.8, 1170.6, 1124.3, 700  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.2-1.65 (17H, m), 1.9-2.1 (4H, m),  
2.3-2.6 (2H, m), 2.55 (4H, t,  $J=5.0\text{Hz}$ ), 3.44 (4H,  
t,  $J=5.0\text{Hz}$ ), 7.1-7.4 (5H, m)

APCI-MASS :  $m/z = 345 (M^+ + H)$

Preparation 319

To a suspension of 1-(N,N-dimethylamino)-2-(4-ethoxycarbonylbenzoyl)ethylene (0.742 g) and 4-n-hexyloxybenzamidinium hydrochloride (0.847 g) in methanol (10 ml) was added 28% sodium methoxide in methanol (0.64 ml). The suspension was refluxed for 6 hours, and partitioned with ethyl acetate and water. The organic layer was washed with water and brine, dried over magnesium sulfate and evaporated under reduced pressure. The residue was triturated with acetonitrile, collected by filtration and dried under reduced pressure to give Methyl 4-[2-(4-n-hexyloxyphenyl)pyrimidin-6-yl]benzoate (0.61 g).

IR (KBr) : 2931, 2861, 1722, 1606, 1558, 1251  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.95 (3H, t,  $J=6.7\text{Hz}$ ), 1.2-1.6 (6H, m), 1.8-2.0 (2H, m), 3.97 (3H, s), 4.05 (2H, t,  $J=6.5\text{Hz}$ ), 7.02 (2H, d,  $J=8.8\text{Hz}$ ), 7.56 (1H, d,  $J=5.2\text{Hz}$ ), 8.18 (2H, d,  $J=8.6\text{Hz}$ ), 8.28 (2H, d,  $J=8.6\text{Hz}$ ), 8.52 (2H, d,  $J=8.8\text{Hz}$ ), 8.83 (1H, d,  $J=5.2\text{Hz}$ )

APCI-MASS :  $m/z = 391 (M + H^+)$

Preparation 320

154

A solution of 1-(4-Methoxycarbonylphenyl)-3-(4-n-pentyloxyphenyl)-1-propen-3-one (4.0 g) and hydroxyamine hydrochloride (3.93 g) in ethanol (40 ml) was refluxed for 4 hours. The mixture was diluted with ethyl acetate, and the organic layer was washed with water (x 2), brine and dried over magnesium sulfate. The solvents were removed under reduced pressure to give crude oxime. To a solution of crude oxime in 1,2-dichloroethane (20 ml) was added activated-manganese(IV) oxide (10.0 g). The reaction mixture was refluxed for 2 hours and filtered. The residue was washed with dichloromethane. The solvents were removed under reduced pressure and the residue was triturated with acetonitrile. The solid was collected by filtration and dried to give Methyl 4-[3-(4-n-pentyloxyphenyl)isoxazol-5-yl]benzoate (0.98 g).

IR (KBr) : 2940, 2871, 1720, 1612, 1278, 1249, 1178, 1108  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.94 (3H, t,  $J=7.2\text{Hz}$ ), 1.2-1.6 (4H, m), 1.7-1.9 (2H, m), 3.95 (3H, s), 4.01 (2H, t,  $J=6.5\text{Hz}$ ), 6.87 (1H, s), 6.98 (2H, d,  $J=8.9\text{Hz}$ ), 7.79 (2H, d,  $J=8.9\text{Hz}$ ), 7.89 (2H, d,  $J=8.6\text{Hz}$ ), 8.15 (2H, d,  $J=8.6\text{Hz}$ )

APCI-MASS :  $m/z = 366$  ( $M+H^+$ )

#### Preparation 321

To a solution of 4-Methoxycarbonylphenylhydroxyimino-methyl chloride (16.98 g) and 4-n-pentyloxyphenylacetylene (18.96 g) in tetrahydrofuran (170 ml) was added triethylamine (14.4 ml) in tetrahydrofuran (140 ml) over a period of 2 hours at  $40^\circ\text{C}$  and the mixture was stirred at  $40^\circ\text{C}$  for 30 minutes. The mixture was diluted with dichloromethane and washed with water and brine. The separated organic layer was dried over magnesium sulfate and evaporated under reduced pressure. The residue was triturated with acetonitrile. The precipitate was collected by filtration and dried to give

155

Methyl 4-[5-(4-n-pentyloxyphenyl)isoxazol-3-yl]benzoate  
(24.56 g).

IR (KBr) : 2942, 2873, 1716, 1616, 1508, 1280,  
1108  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.95 (3H, t,  $J=6.9\text{Hz}$ ), 1.3-1.6 (4H,  
m), 1.8-2.0 (2H, m), 3.95 (3H, s), 4.02 (2H, t,  
 $J=6.5\text{Hz}$ ), 6.74 (1H, s), 6.99 (2H, d,  $J=8.8\text{Hz}$ ), 7.76  
(2H, d,  $J=8.8\text{Hz}$ ), 7.93 (2H, d,  $J=8.5\text{Hz}$ ), 8.14 (2H,  
d,  $J=8.5\text{Hz}$ )

APCI-MASS :  $m/z = 366$  ( $\text{M}+\text{H}^+$ )

#### Preparation 322

To a solution of N-Hydroxy-4-octyloxybenzamidine (1.89  
g) in pyridine (10 ml) was added terephthalic acid monomethyl  
ester chloride (1.67 g) in tetrahydrofuran (15 ml) dropwise  
at  $0^\circ\text{C}$ . The mixture was stirred at room temperature for 15  
minutes, and poured into water. The precipitate was  
collected by filtration, dried and dissolved in pyridine (10  
ml). The solution was refluxed for 1 hour. The reaction  
mixture was diluted with ethyl acetate and washed with 1N  
HCl, water and brine. The separated organic layer was dried  
over magnesium sulfate and the solvents were removed under  
reduced pressure. The residue was triturated with  
acetonitrile and collected by filtration. The solid was  
dried to give Methyl 4-[3-(4-n-hexyloxyphenyl)-1,2,4-  
oxadiazol-5-yl]benzoate (2.27 g).

IR (KBr) : 2950, 2925, 2863, 1720, 1280, 1255  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.92 (3H, t,  $J=6.6\text{Hz}$ ), 1.2-1.9 (8H,  
m), 3.97 (3H, s), 4.03 (2H, d,  $J=6.5\text{Hz}$ ), 7.00 (2H,  
d,  $J=8.9\text{Hz}$ ), 8.09 (2H, d,  $J=8.9\text{Hz}$ ), 8.20 (2H, d,  
 $J=6.6\text{Hz}$ ), 8.28 (2H, d,  $J=6.6\text{Hz}$ )

APCI-MASS :  $m/z = 381$  ( $\text{M}+\text{H}^+$ )

#### Preparation 323

A suspension of 1-(4-n-Hexyloxybenzoyl)-2-(4-

194

methoxycarbonylbenzoyl)hydrazine (1.00 g) in phosphorus  
oxychloride (5 ml) was refluxed for 1 hour. After cooling,  
the solution was concentrated under reduced pressure. The  
residue was poured into ice-water and extracted with  
5 dichloromethane. The organic layer was washed with water,  
brine and dried over magnesium sulfate. The solvents were  
removed under reduced pressure. The residue was triturated  
with acetonitrile, collected by filtration and dried under  
reduced pressure to give Methyl 4-[5-(4-n-hexyloxyphenyl)-  
10 1,3,4-oxadiazole-2-yl]benzoate (761 mg).

IR (KBr) : 2954, 2854, 1724, 1612, 1494, 1280,  
1249  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.91 (3H, t,  $J=6.6\text{Hz}$ ), 1.3-1.6 (6H,  
m), 1.7-1.9 (2H, m), 3.96 (3H, s), 4.04 (2H, t,  
15  $J=6.5\text{Hz}$ ), 7.02 (2H, d,  $J=8.6\text{Hz}$ ), 8.07 (2H, d,  
 $J=8.6\text{Hz}$ ), 8.19 (4H, m)

APCI-MASS :  $m/z = 381$  ( $M+H$ )<sup>+</sup>

The following compounds (Preparations 324 to 327) were  
20 obtained according to a similar manner to that of Preparation  
323.

Preparation 324

Methyl 4-[5-[4-(4-n-propyloxyphenyl)phenyl]-1,3,4-  
25 oxadiazol-2-yl]benzoate

IR (KBr) : 1720, 1614, 1496, 1280, 1103  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.07 (3H, d,  $J=7.5\text{Hz}$ ), 1.84 (2H, tq,  
 $J=6.5$  and  $7.5\text{Hz}$ ), 3.98 (3H, s), 3.99 (2H, t,  
 $J=6.5\text{Hz}$ ), 7.01 (2H, d,  $J=8.8\text{Hz}$ ), 7.60 (2H, d,  
30  $J=8.8\text{Hz}$ ), 7.73 (2H, d,  $J=8.5\text{Hz}$ ), 8.19 (2H, d,  
 $J=8.5\text{Hz}$ ), 8.22 (4H, s)

APCI-MASS :  $m/z = 415$  ( $M+H$ )<sup>+</sup>

Preparation 325

35 Methyl 4-[5-(n-nonyl)-1,3,4-oxadiazol-2-yl]benzoate

157



IR (KBr) : 2915, 2848, 1724, 1569, 1436, 1413,  
1278  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.4\text{Hz}$ ), 1.2-1.6 (12H, m), 1.8-2.0 (2H, m), 2.94 (2H, t,  $J=7.6\text{Hz}$ ), 3.96 (3H, s), 8.11 (2H, d,  $J=8.8\text{Hz}$ ), 8.17 (2H, d,  $J=8.8\text{Hz}$ )

APCI-MASS :  $m/z = 331$  ( $\text{M}+\text{H}^+$ )

Preparation 326

Methyl 4-[5-[4-(8-methoxyoctyloxy)phenyl]-1,3,4-oxadiazol-2-yl]benzoate

IR (KBr) : 2925, 2858, 1722, 1614, 1280, 1259  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.3-1.9 (12H, m), 3.36 (3H, s), 3.37 (2H, t,  $J=6.4\text{Hz}$ ), 3.97 (3H, s), 4.04 (2H, t,  $J=6.5\text{Hz}$ ), 7.02 (2H, d,  $J=8.9\text{Hz}$ ), 8.07 (2H, d,  $J=8.9\text{Hz}$ ), 8.20 (4H, s)

APCI-MASS :  $m/z = 439$  ( $\text{M}+\text{H}^+$ )

Preparation 327

Methyl 4-[5-(4-n-octyloxyphenyl)-1,3,4-oxadiazol-2-yl]benzoate

IR (KBr) : 2923, 2856, 1722, 1614, 1496, 1282,  
1103  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.8\text{Hz}$ ), 1.2-1.6 (10H, m), 1.7-1.9 (2H, m), 3.97 (3H, s), 4.04 (2H, t,  $J=6.5\text{Hz}$ ), 7.03 (2H, d,  $J=8.7\text{Hz}$ ), 8.07 (2H, d,  $J=8.7\text{Hz}$ ), 8.19 (4H, m)

APCI-MASS :  $m/z = 409$  ( $\text{M}+\text{H}^+$ )

Preparation 328

A suspension of 1-(4-Hexyloxybenzoyl)-2-(4-methoxycarbonylbenzoyl)hydrazine (1.0 g) and di-phosphorus pentasulfide (1.28 g) in tetrahydrofuran (15 ml) was stirred at room temperature for 3 hours. The mixture was diluted with water (30 ml), stirred for 30 minutes and extracted with

08809723, 052197  
261250, E270880

158

dichloromethane. The organic layer was washed with brine, dried over magnesium sulfate and evaporated under reduced pressure. The residue was triturated with acetonitrile. The solid was collected by filtration and dried under reduced pressure to give Methyl 4-[5-(4-n-hexyloxyphenyl)-1,3,4-thiadiazol-2-yl]benzoate (816 mg).

IR (KBr) : 2925, 2871, 1722, 1608, 1436, 1276, 1106  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.92 (3H, t,  $J=6.6\text{Hz}$ ), 1.3-2.0 (8H, m), 3.96 (3H, s), 4.03 (2H, t,  $J=6.5\text{Hz}$ ), 6.99 (2H, d,  $J=8.6\text{Hz}$ ), 7.95 (2H, d,  $J=8.4\text{Hz}$ ), 8.16 (2H, d,  $J=8.4\text{Hz}$ )

APCI-MASS :  $m/z = 397$  ( $\text{M}+\text{H}^+$ )

The following compounds (Preparations 329 to 334) were obtained according to a similar manner to that of Preparation 328.

Preparation 329

Methyl 4-[5-[4-(8-methoxyoctyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoate

IR (KBr) : 3210, 2935, 2856, 1718, 1600, 1465, 1280, 1110  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.3-1.6 (10H, m), 1.7-1.9 (2H, m), 3.33 (3H, s), 3.37 (2H, d,  $J=6.4\text{Hz}$ ), 3.96 (3H, s), 4.03 (2H, t,  $J=6.5\text{Hz}$ ), 6.99 (2H, d,  $J=8.9\text{Hz}$ ), 7.94 (2H, d,  $J=8.9\text{Hz}$ ), 8.07 (2H, d,  $J=8.6\text{Hz}$ ), 8.16 (2H, d,  $J=8.6\text{Hz}$ )

APCI-MASS :  $m/z = 455$  ( $\text{M}+\text{H}^+$ )

Preparation 330

Methyl 4-[5-(4-cyclohexylphenyl)-1,3,4-thiadiazol-2-yl]benzoate

IR (KBr) : 2925, 2850, 1716, 1432, 1274, 1108, 997  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.2-1.6 (5H, m), 1.7-2.0 (5H, m),

159

2.58 (1H, m), 3.96 (3H, s), 7.34 (2H, d, J=8.2Hz),  
7.93 (2H, d, J=8.2Hz), 8.07 (2H, d, J=8.6Hz), 8.16  
(2H, d, J=8.6Hz)

APCI-MASS :  $m/z = 379$  ( $M+H^+$ )

5

Preparation 331

Methyl 4-[5-[4-(piperidin-1-yl)phenyl]-1,3,4-thiadiazol-2-yl]benzoate

IR (KBr) : 2940, 2848, 1720, 1602, 1436, 1415, 1276,  
1108  $\text{cm}^{-1}$

10

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.68 (6H, br), 3.34 (4H, br), 3.96  
(3H, s), 6.95 (2H, d, J=8.7Hz), 7.88 (2H, d,  
J=8.7Hz), 8.05 (2H, d, J=8.6Hz), 8.16 (2H, d,  
J=8.6Hz)

15

APCI-MASS :  $m/z = 380$  ( $M+H^+$ )

Preparation 332

Methyl 4-[5-(4-n-octyloxyphenyl)-1,3,4-thiadiazol-2-yl]benzoate

20

IR (KBr) : 2927, 2858, 1720, 1606, 1434, 1276,  
1106  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t, J=6.8Hz), 1.2-1.6 (10H,  
m), 1.7-1.9 (2H, m), 3.96 (3H, s), 4.03 (2H, t,  
J=6.5Hz), 7.00 (2H, d, J=8.9Hz), 7.95 (2H, d,  
J=8.9Hz), 8.06 (2H, d, J=8.4Hz), 8.16 (2H, d,  
J=8.4Hz)

25

APCI-MASS :  $m/z = 425$  ( $M+H^+$ )

Preparation 333

Methyl 4-[5-(4-trans-n-pentylcyclohexyl)-1,3,4-thiadiazol-2-yl]benzoate

30

IR (KBr) : 2923, 2850, 1722, 1440, 1276, 1110  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t, J=6.9Hz), 1.0-1.8 (13H,  
m), 1.92 (2H, d, J=13.4Hz), 2.24 (2H, d, J=12.2Hz),  
3.15 (1H, tt, J=12.2 and 3.5Hz), 3.95 (3H, s), 8.01

35

160

08309723.052197

(2H, dd, J=8.6 and 2.0Hz), 8.13 (2H, dd, J=8.6 and 2.0Hz)

APCI-MASS :  $m/z = 373$  ( $M+H^+$ )

5 Preparation 334

Methyl 4-[5-[4-(4-n-propyloxyphenyl)phenyl]-1,3,4-thiadiazol-2-yl]benzoate

IR (KBr) : 1720, 1540, 1508, 1282  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.07 (3H, t, J=7.5Hz), 1.85 (2H, m),  
10 3.9-4.1 (5H, m), 7.01 (2H, d, J=8.8Hz), 7.59 (2H, d, J=8.8Hz), 7.70 (2H, d, J=8.4Hz), 8.07 (2H, d, J=8.4Hz), 8.1-8.2 (4H, m)

APCI-MASS :  $m/z = 431$  ( $M+H$ )<sup>+</sup>

15 Preparation 335

To a suspension of 4-hexyloxybenzoic acid in oxalyl chloride (10 ml) and dichloromethane (10 ml) was added N,N-dimethylformamide (0.1 ml). The mixture was stirred at room temperature for 2 hours. The solvent was removed under

20 reduced pressure to give crude 4-hexyloxybenzoyl chloride.

To a suspension of Ethyl 3-amino-4-hydroxybenzoate (733 mg) and triethylamine (1.38 ml) and 4-dimethylaminopyridine (DMAP, 10 mg) in methylene chloride (10 ml) was added the

25 solution of 4-hexyloxybenzoyl chloride obtained above in dichloromethane (5 ml) dropwise at 10°C. The reaction mixture was stirred at 10°C for 1.5 hours and diluted with

dichloromethane (20 ml). The solution was washed with  $\text{H}_2\text{O}$  (20 ml), 1N HCl aq. (20 ml x 2),  $\text{H}_2\text{O}$  (20 ml) and brine (20 ml) successively. The organic layer was dried over  $\text{MgSO}_4$  and

30 the solvent was removed under reduced pressure. To the residue was added toluene (15 ml) and p-toluenesulfonic acid (10 mg). The mixture was refluxed for 6 hours and the solvent was removed under reduced pressure. The residue was

35 triturated with acetonitrile, and precipitate was collected with filtration and dried over  $\text{PO}_5$  to give 2-(4-

08809723, 052197

161

Hexyloxyphenyl)-5-ethoxycarbonylbenzoxazole (0.60 g).

IR (KBr) : 2952, 2871, 1712, 1623, 1500, 1294,  
1255  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.92 (3H, t,  $J=6.6\text{Hz}$ ), 1.3-1.6 (9H,  
m), 1.7-1.9 (2H, m), 4.05 (2H, t,  $J=6.5\text{Hz}$ ), 4.42  
(2H, q,  $J=7.1\text{Hz}$ ), 7.03 (2H, d,  $J=6.9\text{Hz}$ ), 7.57 (1H,  
d,  $J=8.6\text{Hz}$ ), 8.08 (1H, dd,  $J=8.6$  and  $1.7\text{Hz}$ ), 8.18  
(2H, d,  $J=6.9\text{Hz}$ ), 8.43 (1H, d,  $J=1.7\text{Hz}$ )

APCI-MASS :  $m/z = 368$  ( $M+H^+$ )

The following compounds (Preparations 336 to 337) were  
obtained according to a similar manner to that of Preparation  
335.

Preparation 336

5-Ethoxycarbonyl-2-(2-octyloxy-pyridin-5-yl)benzoxazole

IR (KBr) : 2933, 2858, 1716, 1623, 1604, 1577, 1467,  
1290, 1213, 1083  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.7\text{Hz}$ ), 1.2-1.5 (10H,  
m), 1.43 (3H, t,  $J=7.1\text{Hz}$ ), 1.7-1.9 (2H, m), 4.3-4.5  
(4H, m), 6.87 (1H, d,  $J=8.7\text{Hz}$ ), 7.60 (1H, d,  
 $J=8.6\text{Hz}$ ), 8.11 (1H, dd,  $J=8.6$  and  $1.6\text{Hz}$ ), 8.37 (1H,  
dd,  $J=8.8$  and  $2.4\text{Hz}$ ), 8.45 (1H, d,  $J=1.6\text{Hz}$ ), 9.03  
(1H, d,  $J=2.4\text{Hz}$ )

APCI-MASS :  $m/z = 397$  ( $M+H^+$ )

Preparation 337

2-[4-(4-Hexylphenyl)phenyl]-5-ethoxycarbonylbenzoxazole

IR (KBr) : 2952, 2871, 1712, 1623, 1500, 1294, 1255,  
1024  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.6\text{Hz}$ ), 1.2-1.5 (6H,  
m), 1.44 (3H, t,  $J=7.1\text{Hz}$ ), 1.6-1.8 (2H, m), 2.67  
(2H, t,  $J=7.3\text{Hz}$ ), 4.43 (2H, q,  $J=7.1\text{Hz}$ ), 7.27 (1H,  
d,  $J=3.7\text{Hz}$ ), 7.32 (1H, s), 7.5-7.7 (3H, m), 7.77  
(2H, d,  $J=8.6\text{Hz}$ ), 8.12 (1H, dd,  $J=8.6$  and  $1.7\text{Hz}$ ),

1162

8.32 (2H, d, J=8.5Hz), 8.48 (1H, d, J=1.2Hz)  
APCI-MASS : m/z = 428 (M+H<sup>+</sup>)

Preparation 338

5 A suspension of 4-[4-(8-bromooctyloxy)phenyl]benzoic  
acid (1 g) in 2,6-dimethylmorpholine (3.06 ml) was refluxed  
for 30 minutes. The reaction mixture was added to a mixture  
of water and ethyl acetate and adjusted to pH 2.0 with conc.  
HCl. The organic layer was taken and dried over magnesium  
10 sulfate. The magnesium sulfate was filtered off, and the  
filtrate was evaporated under reduced pressure to give 4-[4-  
[8-(2,6-dimethylmorpholin-4-yl)octyloxy]phenyl]benzoic acid  
hydrochloride (0.95 g).

IR (KBr) : 2939.0, 1704.8, 1606.4, 1189.9 cm<sup>-1</sup>

15 NMR (DMSO-d<sub>6</sub>, δ) : 1.12 (6H, d, J=6.3Hz), 1.2-1.6  
(10H, m), 1.6-1.9 (4H, m), 2.4-2.7 (2H, m), 2.9-3.1  
(2H, m), 3.8-4.0 (2H, m), 4.02 (2H, t, J=6.3Hz),  
7.04 (2H, d, J=8.8Hz), 7.68 (2H, d, J=8.8Hz), 7.75  
(2H, d, J=8.4Hz), 7.99 (2H, d, J=8.4Hz)

20 APCI-MASS : m/z = 440 (M+H<sup>+</sup>)

Preparation 339

Sodium hydride (60% suspension in mineral oil, 108 mg)  
was added to ethoxyethanol (10 ml), and the solution was  
25 stirred at 60°C for 20 minutes. To the solution was added  
Methyl 4-[4-(8-bromooctyloxy)phenyl]benzoate (1.26 g), and  
the reaction mixture was stirred at 70°C for 2 hours. To the  
reaction mixture was added 10% sodium hydroxide aqueous  
solution (2.4 ml), and the solution was stirred at 70°C for 1  
30 hour. After cooling, the solution was adjusted to pH 2.0  
with 1N hydrochloric acid. The precipitate was collected by  
filtration, and dried to give 4-[4-[8-(2-  
Ethoxyethoxy)octyloxy]phenyl]benzoic acid (1.13 g).

35 IR (KBr) : 2933, 2858, 1685, 1604, 1434, 1294,  
1132 cm<sup>-1</sup>

163

08809723.052197

NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.09 (3H, t,  $J=7.0\text{Hz}$ ), 1.2-1.9 (14H, m), 3.2-3.6 (6H, m), 4.01 (2H, d,  $J=6.3\text{Hz}$ ), 7.04 (2H, d,  $J=8.8\text{Hz}$ ), 7.67 (2H, d,  $J=8.8\text{Hz}$ ), 7.74 (2H, d,  $J=8.5\text{Hz}$ ), 7.98 (2H, d,  $J=8.5\text{Hz}$ )

APCI-MASS :  $m/z = 415$  ( $M+H^+$ )

The following compound was obtained according to a similar manner to that of Preparation 300.

Preparation 340

4-n-Pentyloxybenzoylhydrazine

IR (KBr) : 3182, 2937, 2869, 1645, 1618, 1571, 1251  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (3H, d,  $J=7.1\text{Hz}$ ), 1.2-1.8 (6H, m), 4.00 (2H, t,  $J=6.5\text{Hz}$ ), 4.41 (2H, s), 6.96 (2H, d,  $J=8.8\text{Hz}$ ), 7.78 (2H, d,  $J=8.8\text{Hz}$ ), 9.59 (1H, s)

APCI-MASS :  $m/z = 223$  ( $M+H^+$ )

The following compound was obtained according to a similar manner to that of Preparation 291.

Preparation 341

1-(4-Methoxycarbonylbenzoyl)-2-(4-n-pentyloxybenzoyl)-hydrazine

IR (KBr) : 3234, 2956, 2931, 1724, 1683, 1643, 1610, 1284, 1253  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.9\text{Hz}$ ), 1.2-1.5 (4H, m), 1.6-1.8 (2H, m), 3.90 (3H, s), 4.04 (2H, t,  $J=6.5\text{Hz}$ ), 7.04 (2H, d,  $J=8.8\text{Hz}$ ), 7.90 (2H, d,  $J=8.8\text{Hz}$ ), 8.03 (2H, d,  $J=8.7\text{Hz}$ ), 8.10 (2H, d,  $J=8.7\text{Hz}$ ), 10.42 (1H, s), 10.64 (1H, s)

APCI-MASS :  $m/z = 385$  ( $M+H^+$ )

The following compound was obtained according to a similar manner to that of Preparation 328.

164

Preparation 342

Methyl 4-[5-(4-n-pentyloxyphenyl)thiadiazol-2-yl]benzoate

IR (KBr) : 2940, 2871, 1720, 1606, 1438, 1280  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.95 (3H, t,  $J=7.1\text{Hz}$ ), 1.3-1.6 (4H, m), 1.8-2.0 (2H, m), 3.96 (3H, s), 4.03 (2H, t,  $J=6.5\text{Hz}$ ), 6.99 (2H, d,  $J=8.8\text{Hz}$ ), 7.94 (2H, d,  $J=8.8\text{Hz}$ ), 8.06 (2H, d,  $J=8.7\text{Hz}$ ), 8.16 (2H, d,  $J=8.7\text{Hz}$ )

APCI-MASS :  $m/z = 383$  ( $\text{M}+\text{H}^+$ )

The following compound was obtained according to a similar manner to that of Preparation 32

Preparation 343

4-[5-(4-n-Pentyloxyphenyl)thiadiazol-2-yl]benzoic acid

IR (KBr) : 2954, 2867, 1687, 1602, 1432, 1294, 1255  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.91 (3H, t,  $J=7.0\text{Hz}$ ), 1.3-1.5 (4H, m), 1.7-1.9 (2H, m), 4.07 (2H, t,  $J=6.7\text{Hz}$ ), 7.13 (2H, d,  $J=8.8\text{Hz}$ ), 7.97 (2H, d,  $J=8.8\text{Hz}$ ), 8.07 (4H, s)

APCI-MASS :  $m/z = 369$  ( $\text{M}+\text{H}^+$ )

The following compound was obtained according to a similar manner to that of Preparation 49.

Preparation 344

1-[4-[5-(4-n-Pentyloxyphenyl)thiadiazol-2-yl]benzoyl]-benzotriazole 3-oxide

IR (KBr) : 2948, 2873, 1770, 1602, 1257, 1232  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.95 (3H, t,  $J=7.1\text{Hz}$ ), 1.3-1.6 (4H, m), 1.8-2.0 (2H, m), 4.04 (2H, t,  $J=6.5\text{Hz}$ ), 7.01 (2H, d,  $J=8.1\text{Hz}$ ), 7.4-7.7 (3H, m), 7.97 (2H, d,  $J=8.1\text{Hz}$ ), 8.12 (1H, d,  $J=8.2\text{Hz}$ ), 8.24 (2H, d,

165



J=8.0Hz), 8.40 (2H, d, J=8.0Hz)  
APCI-MASS : m/z = 486 (M+H<sup>+</sup>)

Preparation 345

To a solution of 4-bromobenzaldehyde oxime chloride (647 mg) and 4-n-pentyloxy-phenylacetylene (650 mg) in tetrahydrofuran (7 ml) was added triethylamine (0.5 ml) in tetrahydrofuran (5 ml) dropwise at 40°C. The solution was stirred at 40°C for 30 minutes, poured into water and extracted with ethyl acetate. The organic layer was washed with H<sub>2</sub>O, brine and dried over magnesium sulfate. The solvents were removed under reduced pressure and the residue was triturated with acetonitrile. The precipitate was collected by filtration and dried to give 4-[5-(4-n-pentyloxyphenyl)isoxazol-3-yl]bromobenzene (0.59 g).

IR (KBr) : 2948, 2867, 1612, 1430, 1255 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 0.95 (3H, t, J=6.9Hz), 1.3-1.6 (4H, m), 1.7-1.9 (2H, m), 4.01 (2H, t, J=6.5Hz), 6.66 (1H, s), 6.98 (2H, d, J=8.8Hz), 7.60 (2H, d, J=8.6Hz), 7.7-7.9 (4H, m)

APCI-MASS : m/z = 388 (M+H<sup>+</sup>)

Preparation 346

To a suspension of 4-[5-(4-n-pentyloxyphenyl)isoxazol-3-yl]bromobenzene (386 mg) in tetrahydrofuran (5 ml) was added 1.55M n-butyllithium in hexane (0.84 ml) at -40°C under N<sub>2</sub> stream and the solution was stirred for 1 hour at -40°C. To the solution was added crushed dryice (1 g) and the suspension was stirred for 1 hour at -40°C. The suspension was diluted with H<sub>2</sub>O, and acidified with 1N-hydrochloric acid. The precipitate was collected by filtration and dried to give 4-[5-(4-n-pentyloxyphenyl)isoxazol-3-yl]benzoic acid (312 mg).

IR (KBr) : 2939, 2867, 1681, 1614, 1429, 1255, 1178, 821 cm<sup>-1</sup>

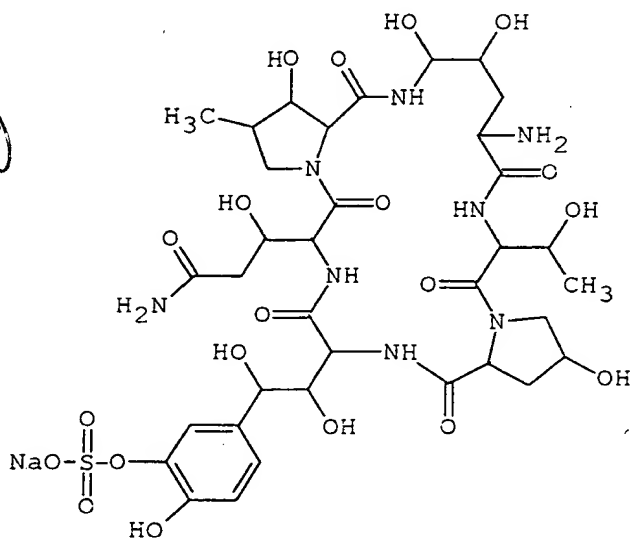
166

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.91 (3H, t, J=7.1Hz), 1.3-1.5 (4H, m), 1.6-1.8 (2H, m), 4.04 (2H, t, J=6.5Hz), 7.11 (2H, d, J=8.9Hz), 7.54 (1H, s), 7.85 (2H, d, J=8.9Hz), 7.98 (2H, d, J=8.6Hz), 8.11 (2H, d, J=8.6Hz)

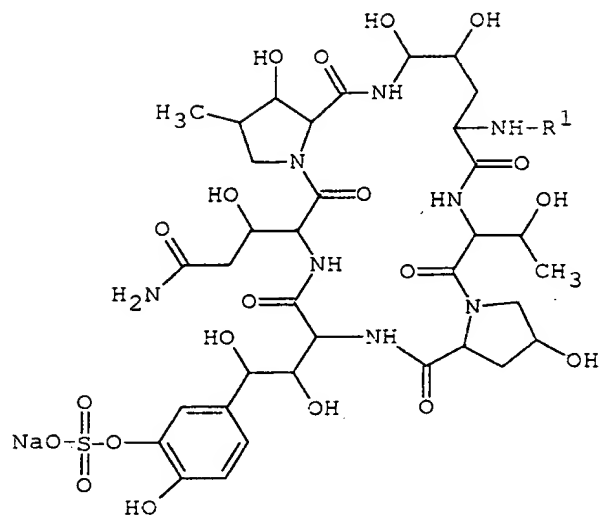
APCI-MASS : m/z = 352 (M+H<sup>+</sup>)

The Starting Compound in the following Examples 1 to 117 and The Object Compounds (1) to (122) and (124) in the following Examples 1 to 122 and 124 are illustrated by chemical formulae as below.

The Starting Compound  
(the same in  
Examples 1 to 117)



The Object Compounds (1) to (122) and (124)



20

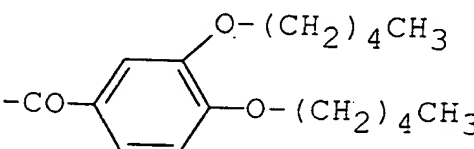
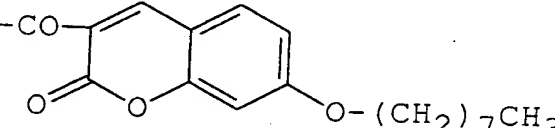
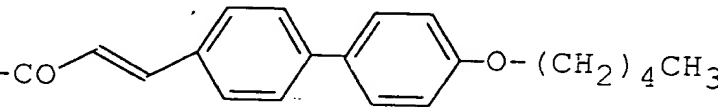
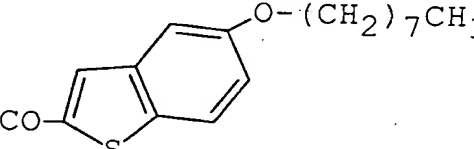
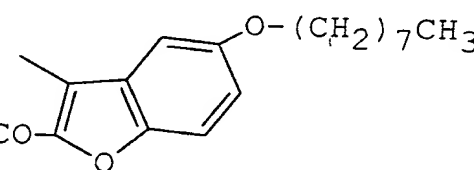
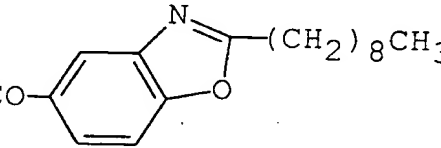
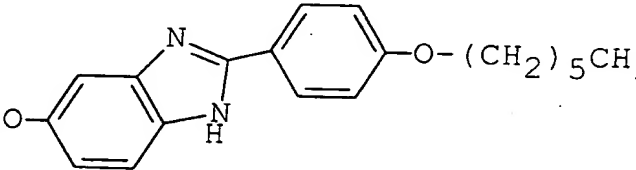
In the following Examples, The Object Compound (X)  
[e.g. The Object Compound (1)] means the object compound of  
Example (X) [e.g. Example (1)].

168

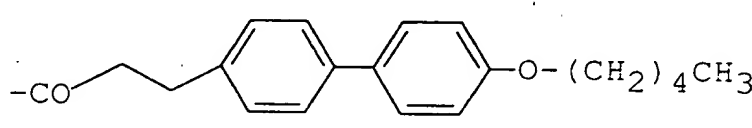
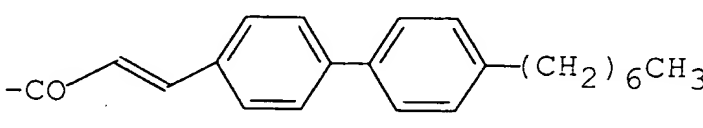
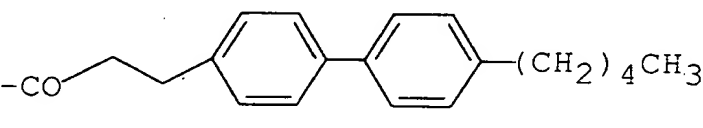
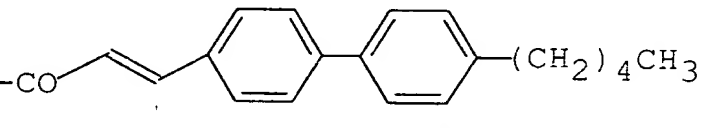
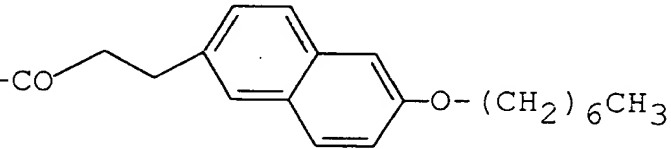
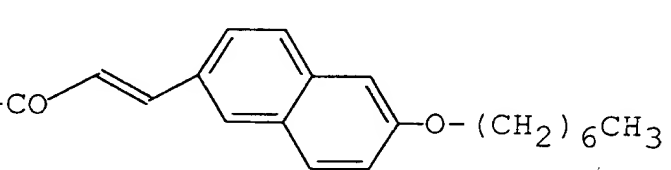
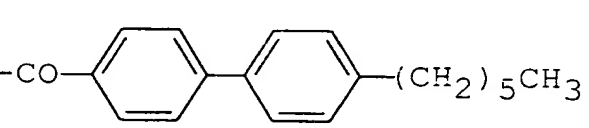
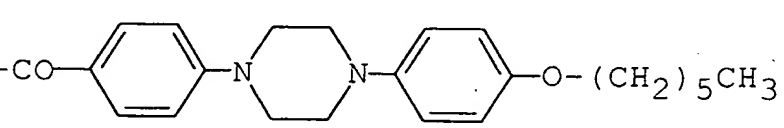
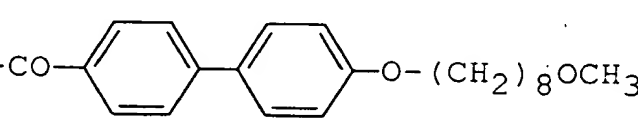
T, 1690

Example No.	R <sup>1</sup>
1	
2	
3	
4	
5	
6	
7	
8	

169

Example No.	$R^1$
9	
10	
11	
12	
13	
14	
15	

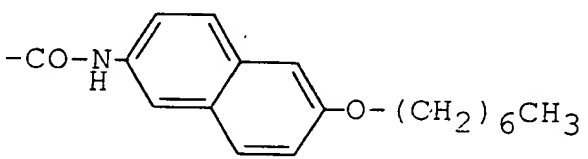
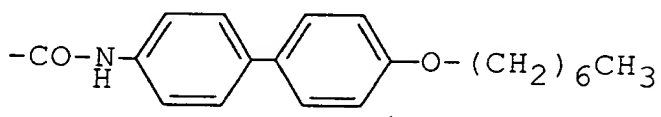
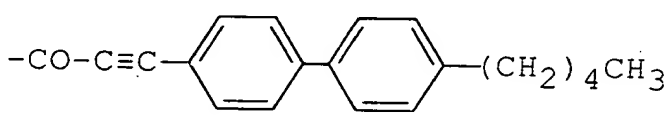
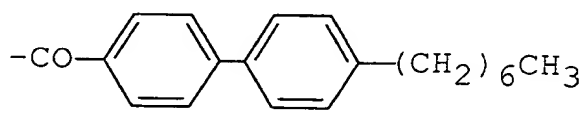
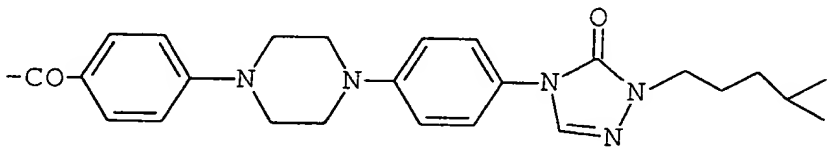
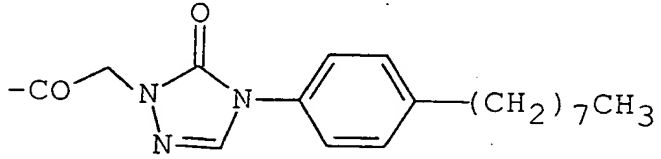
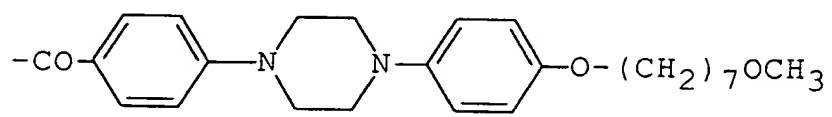
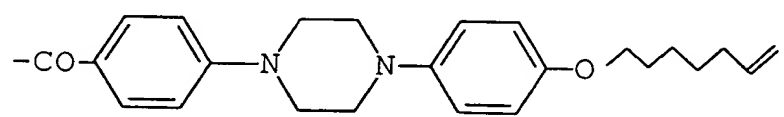
170

Example No.	R <sup>1</sup>
16	
17	
18	
19	
20	
21	
22	
23	
24 major product	

171

Example No.	R <sup>1</sup>
24 minor product	<chem>-CO-c1ccc(cc1)-c2ccc(cc2)OCCCCC=C</chem>
25	<chem>-CO-c1ccc(cc1)-c2ccoc2-c3ccc(cc3)OCCCC</chem>
26	<chem>-CO-N1CCN(CC1)-c2ccc(cc2)OCCCCC</chem>
27	<chem>-CO-CH2-O-c1ccc(cc1)OCCCCC</chem>
28	<chem>-CO-C1CCN(C1)C(=O)-c2ccc3ccccc3c2OCCCCC</chem>
29	<chem>-CO-c1ccc2c(c1)c(c[nH]2)C(=N)CCCCC</chem>
30	<chem>-CO-c1ccncc1OCCCCC</chem>
31	<chem>-CO-C#Cc1ccc2ccccc2c1OCCCCC</chem>

172

Example No.	R <sup>1</sup>
32	
33	
34	
35	
36	
37	
38 major product	
38 minor product	

173

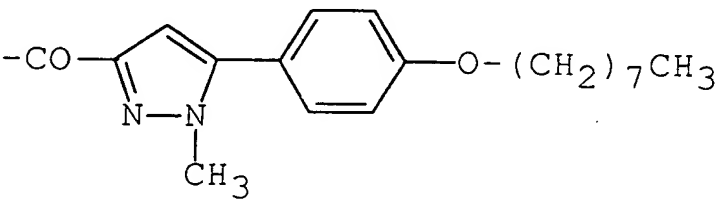
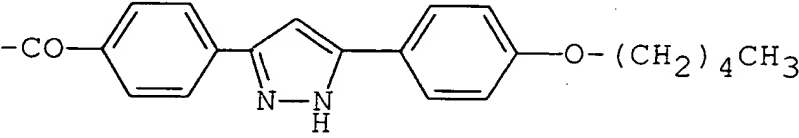
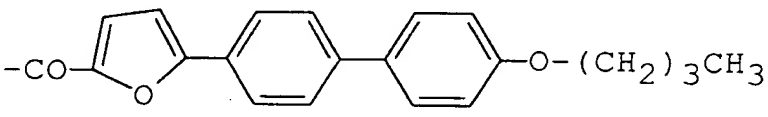
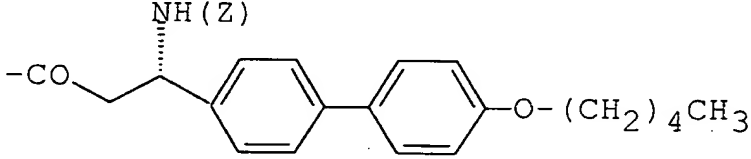
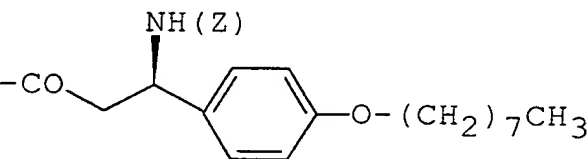
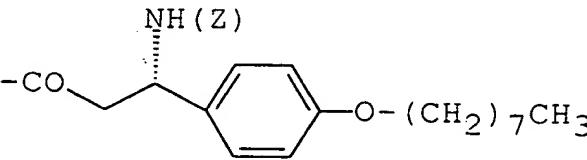


Example No.	R <sup>1</sup>
39	
40	
41	
42 mixture product	
43	
44	
45	
46	

176

Example No.	R <sup>1</sup>
47	
48	
49	
50	
51	
52	
53	

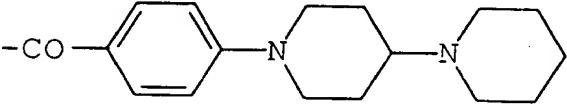
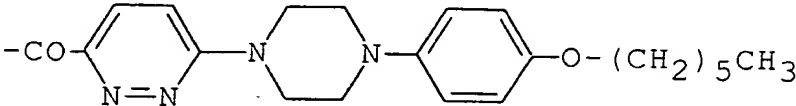
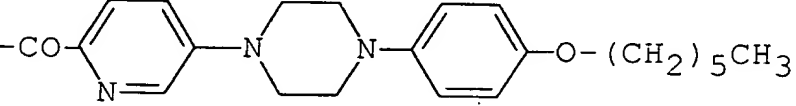
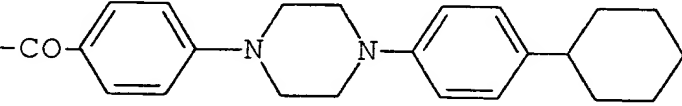
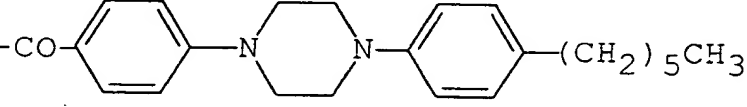
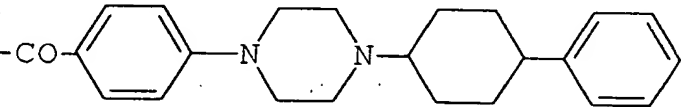
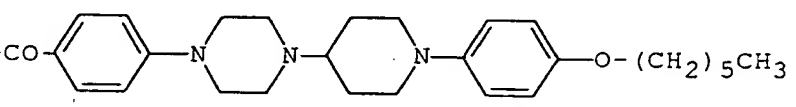
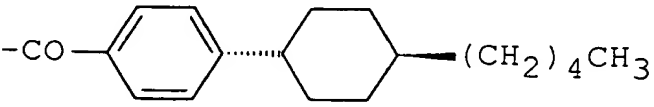
175

Example No.	$R^1$
54	
55	
56	
57	
58	
59	

174

Example No.	R <sup>1</sup>
60	<chem>CCCCCCCCCCCCCCCC(=O)C(O)Cc1ccccc1</chem>
61	<chem>CCCCCCCCCCCCCCCCOC[C@H](NC(=O)O)CC(=O)O</chem>
62	<chem>CCCCCCCCCCCCCCC(O)CC(=O)O</chem>
63	<chem>CCCCCCCCCCCCC(C)=CC(=O)O</chem>
64 major product	<chem>CCCCCCCCCOc1ccc(cc1)N2CCN(CC2)c3ccc(cc3)C(=O)O</chem>
64 minor product	<chem>CCCCCCCCCOc1ccc(cc1)N2CCN(CC2)c3ccc(cc3)C(=O)O</chem>
65	<chem>CCCCCOc1ccc(cc1)N2CCN(CC2)c3ccc(cc3)C(=O)O</chem>
66	<chem>CCCCCOc1ccc(cc1)N2CCN(CC2)c3ccc(cc3)C(=O)O</chem>

177

Example No.	R <sup>1</sup>
67	
68	
69	
70	
71	
72	
73	
74	

174

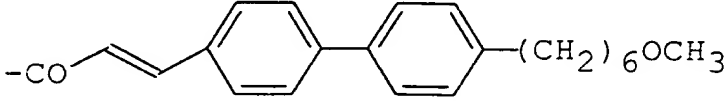
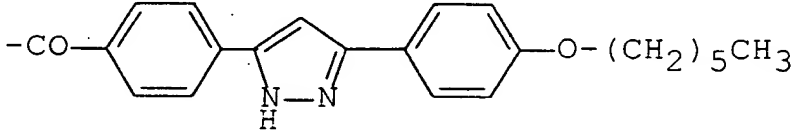
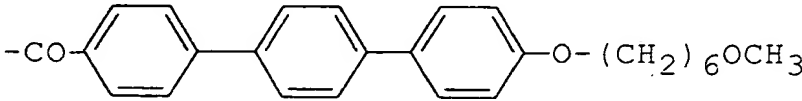
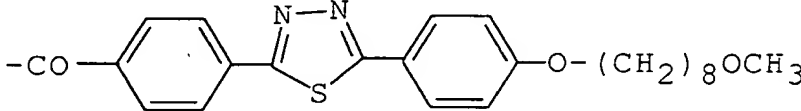
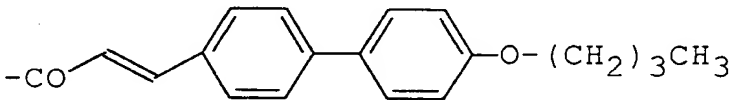
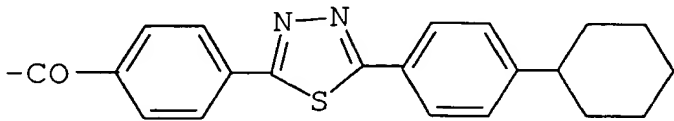
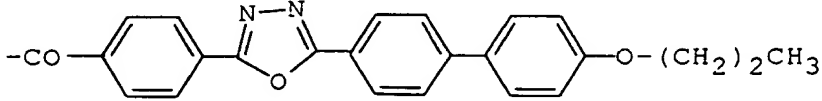
Example No.	R <sup>1</sup>
75	
76	
77	
78	
79	
80	

08809723.052197  
/67250"E260880

179

Example No.	$R^1$
81	<chem>-CO-c1ccc2ccccc2c1-(CH2)6CH3</chem>
82	<chem>-CO-c1ccc2ccccc2c1-(CH2)5CH3</chem>
83	<chem>-CO/C=C/c1ccc(cc1)-c2ccc(cc2)OCCCCCCCCOC</chem>
84	<chem>-CO/C=C/c1ccc(cc1)-c2ccc(cc2)OCCCCC=C</chem>
85	<chem>-CO/C=C/c1ccc(cc1)-c2ccc(cc2)OCCCC(C)C</chem>
86	<chem>-CO/C=C/c1ccc(cc1)-c2ccc(cc2)OCCCCCCCCI</chem>

180

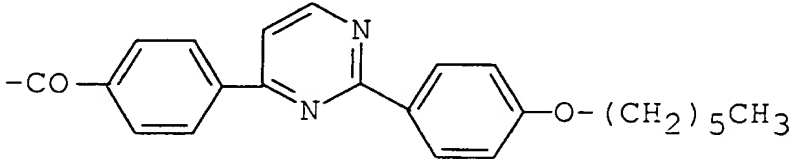
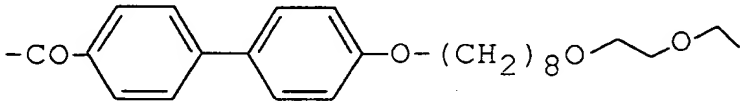
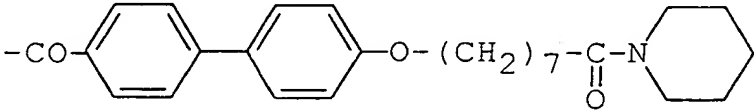
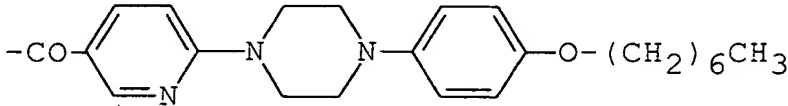
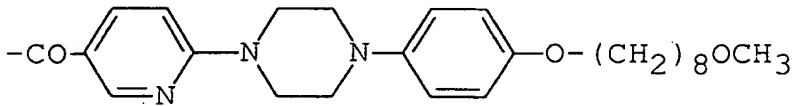
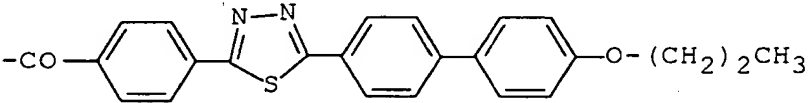
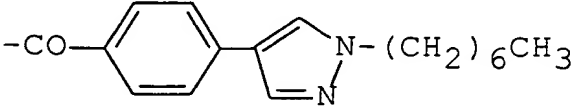
Example No.	R <sup>1</sup>
87	
88	
89	
90	
91	
92	
93	

148



Example No.	R <sup>1</sup>
94	
95	
96	
97	
98	
99	
100	
101	

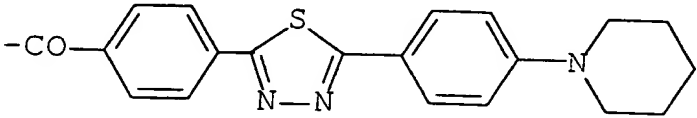
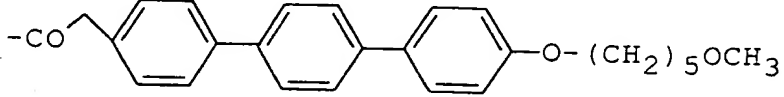
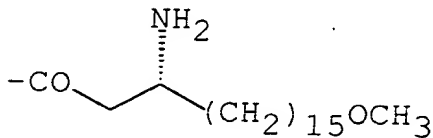
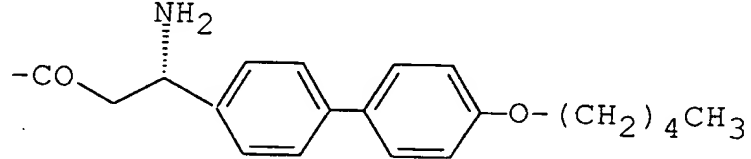
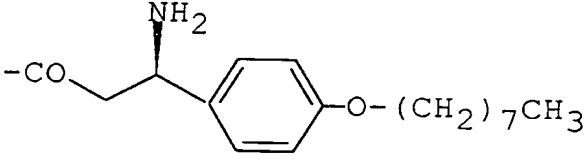
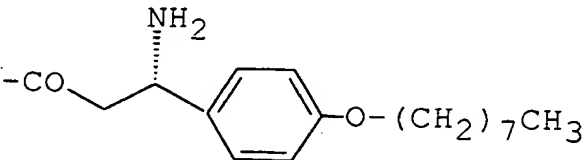
182

Example No.	R <sup>1</sup>
102	
103	
104	
105	
106	
107	
108	

183

Example No.	$R^1$
109	<chem>CC(CCCCOc1ccc(cc1)-c2ccoc(=O)c2)C(=O)O</chem>
110	<chem>CCCCOc1ccc(cc1)-c2ccc(cc2)C(=O)O</chem>
111	<chem>COCC(CCCCOc1ccc(cc1)-c2ccc(cc2)/C=C/C(=O)O)C(=O)O</chem>
112	<chem>C1CCOCC1OCC(CCCCOc1ccc(cc1)-c2ccc(cc2)C(=O)O)C(=O)O</chem>
113	<chem>CCCCCCCCCN1C=Cc2ccccc2C1C(=O)O</chem>
114	<chem>CCCCCOCC(CCCCOc1ccc(cc1)-c2ccc(cc2)C(=O)O)C(=O)O</chem>
115	<chem>COCC(CCCCOc1ccc(cc1)-c2ccc(cc2)-c3ccc(cc3)C(=O)O)C(=O)O</chem>

184

Example No.	R <sup>1</sup>
116	
117	
118	
119	
120	
121	

185

Example No.	R <sup>1</sup>
122	<chem>CCCOCCc1ccc(cc1)-c2ccc(cc2)/C=C/C(=O)O</chem>

Example No.	The Object Compound
123	

Example No.	R <sup>1</sup>
124	<chem>CCCOCCc1ccc(cc1)-c2nn(s2)-c3ccc(cc3)C(=O)O</chem>

146

Example 1

To a solution of The Starting Compound (1 g) and 1-(6-octyl-oxymethylpicolinoyl)benzotriazole 3-oxide (0.399 g) in N,N-dimethylformamide (10 ml) was added 4-(N,N-dimethylamino)pyridine (0.140 g), and stirred for 12 hours at ambient temperature. The reaction mixture was pulverized with ethyl acetate. The precipitate was collected by filtration, and dried under reduced pressure. The powder was dissolved in water, and subjected to column chromatography on ion exchange resin (DOWEX-50WX4 (Trademark : prepared by Dow Chemical)) eluting with water. The fractions containing the object compound were combined, and subjected to column chromatography on ODS (YMC-gel-ODS-AM-S-50) (Trademark : prepared by Yamamura Chemical Lab.) eluting with 50% methanol aqueous solution. The fractions containing the object compound were combined, and evaporated under reduced pressure to remove methanol. The residue was lyophilized to give The Object Compound (1).

IR (KBr) : 3347, 1664, 1629, 1517  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.7\text{Hz}$ ), 0.98 (3H, d,  $J=6.7\text{Hz}$ ), 1.09 (3H, d,  $J=6.0\text{Hz}$ ), 1.2-1.47 (10H, m), 1.47-1.67 (2H, m), 1.67-2.06 (3H, m), 2.06-2.5 (4H, m), 3.19 (1H, m), 3.53 (2H, t,  $J=6.4\text{Hz}$ ), 3.5-3.85 (2H, m), 3.85-4.7 (13H, m), 5.35 (11H, m), 5.56 (1H, d,  $J=5.7\text{Hz}$ ), 6.73 (1H, d,  $J=8.3\text{Hz}$ ), 6.83 (1H, d,  $J=8.3\text{Hz}$ ), 6.89 (1H, s), 7.05 (1H, s), 7.11 (1H, s), 7.32 (1H, m), 7.43 (1H, d,  $J=8.5\text{Hz}$ ), 7.63 (1H, d,  $J=7.3\text{Hz}$ ), 7.85-8.13 (4H, m), 8.66 (1H, d,  $J=7.8\text{Hz}$ ), 8.84 (1H, s)

FAB-MASS :  $m/z = 1228$  ( $\text{M}^+ + \text{Na}$ )

Elemental Analysis Calcd. for  $\text{C}_{50}\text{H}_{72}\text{N}_9\text{O}_{22}\text{SNa} \cdot 6\text{H}_2\text{O}$  :

C 45.49, H 6.44, N 9.59

Found : C 45.89, H 6.52, N 9.69

187

The Object Compounds (2) to (25) were obtained according to a similar manner to that of Example 1.

Example 2

5 IR (KBr) : 3353, 1666, 1510, 1236  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.7\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.06 (3H, d,  $J=5.8\text{Hz}$ ), 1.2-1.5 (10H, m), 1.55-2.05 (5H, m), 2.11-2.7 (4H, m), 3.0-3.3 (5H, m), 3.3-3.5 (4H, m), 3.6-4.5 (15H, m), 4.6-5.6 (12H, m), 6.6-7.2 (10H, m), 7.2-7.5 (3H, m), 7.81 (2H, d,  $J=8.8\text{Hz}$ ), 8.05 (1H, d,  $J=8.7\text{Hz}$ ), 8.28 (1H, d,  $J=8.7\text{Hz}$ ), 8.41 (1H, d,  $J=6.7\text{Hz}$ ), 8.84 (1H, s)  
FAB-MASS :  $m/z = 1373$  ( $\text{M}^+ + \text{Na}$ )  
15 Elemental Analysis Calcd. for  $\text{C}_{60}\text{H}_{83}\text{N}_{10}\text{O}_{22}\text{SNa} \cdot 4\text{H}_2\text{O}$  :  
C 50.63, H 6.44, N 9.84  
Found : C 50.59, H 6.59, N 9.79

Example 3

20 IR (KBr) : 3350, 1664, 1627, 1047  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.6\text{Hz}$ ), 1.08 (3H, d,  $J=5.7\text{Hz}$ ), 1.15-1.53 (8H, m), 1.55-2.1 (9H, m), 2.1-2.45 (3H, m), 2.5-2.7 (1H, m), 3.18 (1H, m), 3.6-3.83 (2H, m), 3.83-4.6 (17H, m), 4.7-5.4 (11H, m), 5.51 (1H, d,  $J=5.9\text{Hz}$ ), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.83 (1H, d,  $J=8.2\text{Hz}$ ), 6.85 (1H, s), 7.03 (2H, d,  $J=8.4\text{Hz}$ ), 7.05 (1H, s), 7.30 (1H, s), 7.2-7.5 (2H, m), 7.67 (2H, d,  $J=8.4\text{Hz}$ ), 7.71 (2H, d,  $J=7.4\text{Hz}$ ), 7.94 (1H, s), 7.96 (2H, d,  $J=7.4\text{Hz}$ ), 8.06 (1H, d,  $J=8.0\text{Hz}$ ), 8.25 (1H, d,  $J=6.7\text{Hz}$ ), 8.50 (1H, s), 8.74 (1H, d,  $J=6.7\text{Hz}$ ), 8.84 (1H, s)  
25 FAB-MASS :  $m/z = 1356$  ( $\text{M}^+ + \text{Na}$ )  
30 Elemental Analysis Calcd. for  $\text{C}_{58}\text{H}_{76}\text{N}_{11}\text{O}_{22}\text{SNa} \cdot 4\text{H}_2\text{O}$  :  
35 C 49.53, H 6.02, N 10.95

168

Found : C 49.26, H 6.22, N 10.77

Example 4

IR (KBr) : 3350, 1660, 1631, 1047  $\text{cm}^{-1}$

5 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.9\text{Hz}$ ), 0.97 (3H, d,  $J=6.6\text{Hz}$ ), 1.09 (3H, d,  $J=5.3\text{Hz}$ ), 1.2-1.5 (10H, m), 1.37 (6H, s), 1.55-2.0 (5H, m), 2.1-2.6 (4H, m), 3.16 (1H, m), 3.73 (2H, m), 3.89 (2H, t,  $J=6.3\text{Hz}$ ), 3.95-4.49 (11H, m), 4.68-5.21 (10H, m), 5.25 (1H, d,  $J=4.1\text{Hz}$ ), 5.53 (1H, d,  $J=5.7\text{Hz}$ ), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.75-6.85 (4H, m), 6.91 (1H, d,  $J=8.2\text{Hz}$ ), 7.05 (1H, s), 7.15 (1H, s), 7.3-7.5 (2H, m), 7.9-8.2 (3H, m), 8.84 (1H, s)

15 FAB-MASS :  $m/z = 1271$  ( $M^+ + \text{Na}$ )

Elemental Analysis Calcd. For  $\text{C}_{53}\text{H}_{77}\text{N}_8\text{O}_{23}\text{SNa} \cdot 4\text{H}_2\text{O}$  :

C 48.18, H 6.48, N 8.48

Found : C 48.04, H 6.51, N 8.38

20 Example 5

IR (KBr) : 1666, 1629, 1222  $\text{cm}^{-1}$

25 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.6\text{Hz}$ ), 0.9-1.12 (6H, m), 1.12-1.52 (13H, m), 1.52-1.93 (5H, m), 2.08-2.55 (4H, m), 3.16 (1H, m), 3.6-5.3 (26H, m), 5.49 + 5.54 (1H, d,  $J=5.8\text{Hz}$ , mixture of diastereomer), 6.60-7.1 (7H, m), 7.04 (1H, s), 7.1 (1H, m), 7.2-7.5 (2H, m), 7.9-8.43 (3H, m), 8.83 (1H, s)

FAB-MASS :  $m/z = 1257$  ( $M^+ + \text{Na}$ )

30 Elemental Analysis Calcd. for  $\text{C}_{52}\text{H}_{75}\text{N}_8\text{O}_{23}\text{SNa} \cdot 3\text{H}_2\text{O}$  :

C 48.44, H 6.33, N 8.69

Found : C 48.16, H 6.51, N 8.53

Example 6

35 IR (KBr) : 3349, 1666, 1629, 1259  $\text{cm}^{-1}$

149



NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.86 (3H, t, J=6.7Hz), 0.9 (3H, d, J=5.7Hz), 0.96 (3H, d, J=6.7Hz), 1.1-1.55 (19H, m), 1.55-2.0 (5H, m), 2.0-2.47 (4H, m), 2.65-3.25 (3H, m), 3.5-5.13 (27H, m), 5.17 (1H, d, J=3.2Hz), 5.24 (1H, d, J=4.5Hz), 5.38 (1H, d, J=5.9Hz), 6.5-6.9 (5H, m), 6.9-7.1 (3H, m), 7.2-7.46 (2H, m), 7.7-8.1 (3H, m), 8.83 (1H, s)

FAB-MASS : m/z = 1368 (M<sup>+</sup>+Na)

Elemental Analysis Calcd. for C<sub>58</sub>H<sub>84</sub>N<sub>9</sub>O<sub>24</sub>SNa·5H<sub>2</sub>O :

C 48.50, N 6.60, N 8.78

Found : C 48.47, H 6.83, N 8.78

#### Example 7

IR (KBr) : 3350, 1666, 1502, 1199 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.86 (3H, t, J=6.6Hz), 0.97 (3H, d, J=6.7Hz), 1.06 (3H, d, J=5.7Hz), 1.2-1.5 (10H, m), 1.55-2.0 (5H, m), 2.1-2.6 (4H, m), 3.17 (1H, m), 3.7-4.5 (15H, m), 4.7-5.22 (10H, m), 5.24 (1H, d, J=4.4Hz), 5.60 (1H, d, J=5.9Hz), 6.68-7.03 (8H, m), 7.04 (1H, s), 7.2-7.42 (2H, m), 7.85-8.1 (3H, m), 8.83 (1H, s)

FAB-MASS : m/z = 1229 (M<sup>+</sup>+Na)

Elemental Analysis Calcd. for C<sub>50</sub>H<sub>71</sub>N<sub>8</sub>O<sub>23</sub>SNa·5H<sub>2</sub>O :

C 46.29, H 6.29, N 8.64

Found : C 46.39, H 6.05, N 8.72

#### Example 8

IR (KBr) : 3350, 1666, 1631, 1513 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.88 (3H, t, J=6.2Hz), 0.97 (3H, d, J=6.7Hz), 1.04 (3H, d, J=5.7Hz), 1.2-1.58 (8H, m), 1.58-2.0 (5H, m), 2.0-2.6 (4H, m), 3.17 (1H, m), 3.6-4.5 (15H, m), 4.63-5.33 (13H, m), 5.53 (1H, d, J=5.9Hz), 6.73 (1H, d, J=8.2Hz), 6.82 (1H, d, J=8.2Hz), 6.84 (1H, s), 6.95-7.52 (7H, m), 7.66 (1H, d, J=7.6Hz), 7.7-7.9 (3H, m),

190

8.05 (1H, d, J=9.1Hz), 8.15 (1H, d, J=7.6Hz),  
8.85 (1H, s)

FAB-MASS :  $m/z = 1279$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{54}H_{73}N_8O_{23}SNa \cdot 5H_2O$  :

C 48.14, H 6.21, N 8.32

Found : C 48.43, H 6.28, N 8.30

Example 9

IR (KBr) : 3347, 2956, 1664, 1633, 1508, 1444, 1268,  
1047  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.9-1.1 (9H, m), 1.06 (3H, d,  
J=5.9Hz), 1.3-1.5 (8H, m), 1.6-2.0 (7H, m), 2.1-  
2.4 (3H, m), 2.5-2.6 (1H, m), 3.1-3.3 (1H, m),  
3.6-4.4 (17H, m), 4.7-5.0 (8H, m), 5.09 (1H, d,  
J=5.5Hz), 5.16 (1H, d, J=3.1Hz), 5.24 (1H, d,  
J=4.5Hz), 6.73 (1H, d, J=8.2Hz), 6.8-6.9 (2H,  
m), 6.98 (1H, d, J=8.3Hz), 7.05 (1H, d,  
J=1.7Hz), 7.3-7.6 (5H, m), 8.08 (1H, d,  
J=8.9Hz), 8.25 (1H, d, J=8.4Hz), 8.54 (1H, d,  
J=7.5Hz), 8.83 (1H, s)

FAB-MASS :  $m/z = 1257$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{52}H_{75}N_8O_{23}SNa \cdot 4H_2O$  :

C 47.78, H 6.40, N 8.57

Found : C 47.88, H 6.71, N 8.53

Example 10

IR (KBr) : 3350, 2931, 1664, 1625, 1529, 1440, 1276,  
1226, 1047  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t, J=6.8Hz), 0.97 (3H,  
d, J=6.7Hz), 1.12 (3H, d, J=5.9Hz), 1.2-1.5  
(10H, m), 1.6-2.1 (5H, m), 2.1-2.4 (4H, m), 3.1-  
3.3 (1H, m), 3.5-4.6 (15H, m), 4.7-5.0 (3H, m),  
5.0-5.2 (7H, m), 5.27 (1H, d, J=4.4Hz), 5.55  
(1H, d, J=5.7Hz), 6.73 (1H, d, J=8.2Hz), 6.8-7.0  
(2H, m), 7.0-7.2 (4H, m), 7.3-7.6 (2H, m), 7.90

191

(1H, d, J=8.8Hz), 8.0-8.2 (2H, m), 8.8-8.9 (2H, m), 9.06 (1H, d, J=7.2Hz)

FAB-MASS :  $m/z = 1281$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{53}H_{71}N_8O_{24}SNa \cdot 5H_2O$  :

C 47.18, H 6.05, N 8.30

Found : C 46.97, H 6.27, N 8.22

Example 11

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.87-1.05 (6H, m), 1.10 (3H, d, J=5.7Hz), 1.3-1.5 (4H, m), 1.6-1.9 (5H, m), 2.2-2.5 (3H, m), 2.6 (1H, m), 3.1-3.2 (1H, m), 3.7-4.5 (15H, m), 4.8-5.1 (8H, m), 5.09 (1H, d, J=5.64Hz), 5.16 (1H, d, J=3.2Hz), 5.26 (1H, d, J=4.2Hz), 5.52 (1H, d, J=6.0Hz), 6.73 (2H, d, J=8.4Hz), 6.8-6.9 (2H, m), 7.0-7.1 (3H, m), 7.2-7.4 (4H, m), 7.6-7.8 (6H, m), 8.11 (1H, d, J=8.4Hz), 8.29 (1H, d, J=8.4Hz), 8.51 (1H, d, J=7.7Hz), 8.85 (1H, s)

FAB-MASS :  $m/z = 1273$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{55}H_{71}N_8O_{22}SNa \cdot 4H_2O$  :

C 49.92, H 6.02, N 8.47

Found : C 49.79, H 6.14, N 8.45

Example 12

IR (KBr) : 3330, 2929, 1670, 1629, 1533, 1440, 1280, 1226, 1045, 804  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t, J=6.7Hz), 0.97 (3H, d, J=6.7Hz), 1.08 (3H, d, J=5.9Hz), 1.2-1.6 (10H, m), 1.6-2.0 (5H, m), 2.1-2.5 (4H, m), 3.1-3.3 (1H, m), 3.6-4.5 (15H, m), 4.8-5.1 (9H, m), 5.17 (1H, d, J=3.0Hz), 5.25 (1H, d, J=4.5Hz), 5.56 (1H, d, J=5.6Hz), 6.73 (1H, d, J=8.2Hz), 6.83 (1H, d, J=6.8Hz), 7.1-7.2 (3H, m), 7.3-7.5 (3H, m), 7.85 (1H, d, J=8.8Hz), 8.0-8.2 (3H, m), 8.84 (1H, s), 8.96 (1H, d, J=7.2Hz)

192

FAB-MASS :  $m/z = 1269$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{52}H_{71}N_8O_{22}S_2Na \cdot 4H_2O$  :

C 47.34, H 6.04, N 8.49

Found : C 47.21, H 5.96, N 8.41

5

Example 13

IR (KBr) : 3345, 2927, 1664, 1629, 1515, 1442,  
1274, 1047  $cm^{-1}$

10

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.7Hz$ ), 0.97 (3H,  
d,  $J=6.7Hz$ ), 1.10 (3H, d,  $J=5.9Hz$ ), 1.2-1.4  
(10H, m), 1.5-2.5 (8H, m), 2.46 (3H, s), 2.69  
(2H, t,  $J=7.7Hz$ ), 3.1-3.4 (2H, m), 3.6-4.5 (17H,  
m), 4.8-5.2 (8H, m), 6.7-7.0 (3H, m), 7.05 (1H,  
d,  $J=1.7Hz$ ), 7.14 (1H, s), 7.3-7.6 (5H, m), 8.0-  
8.2 (2H, m), 8.47 (1H, d,  $J=7.0Hz$ ), 8.84 (1H, s)

15

FAB-MASS :  $m/z = 1251$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{53}H_{73}N_8O_{22}SNa \cdot 3H_2O$  :

C 49.61, H 6.21, N 8.73

Found : C 49.88, H 6.44, N 8.74

20

Example 14

IR (KBr) : 3340, 1672, 1627, 1542, 1513, 1440, 1268,  
1045  $cm^{-1}$

25

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.84 (3H, t,  $J=6.7Hz$ ), 0.94 (3H,  
d,  $J=6.7Hz$ ), 1.07 (3H, d,  $J=6.0Hz$ ), 1.2-1.4  
(12H, m), 1.6-2.0 (5H, m), 2.1-2.4 (3H, m), 2.6  
(1H, m), 2.96 (2H, t,  $J=7.4Hz$ ), 3.1-3.3 (1H, m),  
3.6-4.5 (13H, m), 4.7-5.2 (11H, m), 5.50 (1H, d,  
 $J=5.7Hz$ ), 6.73 (1H, d,  $J=8.2Hz$ ), 6.8-6.9 (2H,  
m), 7.04 (1H, s), 7.2-7.5 (3H, m), 7.72 (1H, d,  
 $J=8.5Hz$ ), 7.91 (1H, d,  $J=8.4Hz$ ), 8.05 (1H, d,  
 $J=8.4Hz$ ), 8.2-8.4 (1H, m), 8.80 (1H, d,  
 $J=7.7Hz$ ), 8.83 (1H, s)

30

FAB-MASS :  $m/z = 1252$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{52}H_{72}N_9O_{22}SNa \cdot 6H_2O$  :

35

193

C 46.67, H 6.33, N 9.42

Found : C 46.72, H 6.53, N 9.45

Example 15

5 IR (KBr) : 3350, 2935, 1664, 1627, 1517, 1446, 1251,  
1045  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.90-1.1 (6H, m), 1.10 (3H, d,  
J=5.9Hz), 1.2-1.4 (6H, m), 1.6-2.4 (8H, m), 2.6-  
2.7 (1H, m), 3.1-3.3 (1H, m), 3.7-4.5 (16H, m),  
10 4.7-5.4 (11H, m), 5.51 (1H, d, J=5.6Hz), 6.7-7.0  
(3H, m), 7.0-7.6 (7H, m), 7.74 (1H, d, J=8.6Hz),  
8.0-8.4 (5H, m), 8.7-8.8 (1H, m), 8.84 (1H, s)

FAB-MASS :  $m/z$  = 1301 ( $M^+$ +Na)

Elemental Analysis Calcd. for  $\text{C}_{55}\text{H}_{71}\text{N}_{10}\text{O}_{22}\text{SNa}\cdot 6\text{H}_2\text{O}$  :

15 C 47.62, H 6.03, N 10.01

Found : C 47.65, H 6.03, N 10.03

Example 16

IR (Nujol) : 3353, 1668, 1627, 1540, 1515, 1500  $\text{cm}^{-1}$

20 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.80-1.00 (6H, m), 1.06 (3H, d,  
J=5.9Hz), 1.20-1.53 (4H, m), 1.60-1.95 (5H, m),  
2.00-2.65 (8H, m), 2.80 (2H, t, J=7.5Hz), 3.05-  
3.45 (1H, m), 3.50-3.85 (2H, m), 3.90-4.48 (11H,  
m), 4.65-5.38 (11H, m), 5.47 (1H, d, J=6.0Hz),  
25 6.65-6.90 (2H, m), 6.90-7.10 (2H, m), 7.10-7.65  
(11H, m), 7.90-8.25 (2H, m), 8.30 (1H, d,  
J=7.8Hz), 8.84 (1H, s)

FAB-MASS :  $m/z$  = 1275.3 ( $M^+$ +Na)

Elemental Analysis Calcd. for  $\text{C}_{55}\text{H}_{73}\text{N}_8\text{O}_{22}\text{SNa}\cdot 3\text{H}_2\text{O}$  :

30 C 50.53, H 6.09, N 8.57

Found : C 50.48, H 6.39, N 8.57

Example 17

IR (Nujol) : 3351, 1656, 1623, 1538, 1515  $\text{cm}^{-1}$

35 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t, J=6.7Hz), 0.96 (3H,

194

d, J=6.7Hz), 1.08 (3H, d, J=5.8Hz), 1.15-1.40  
(8H, m), 1.50-2.00 (5H, m), 2.10-2.48 (4H, m),  
2.52-2.70 (2H, m), 3.05-3.28 (1H, m), 3.60-4.50  
(13H, m), 4.70-5.20 (9H, m), 5.25 (1H, d,  
J=4.6Hz), 5.52 (1H, d, J=6.0Hz), 6.68-6.92 (4H,  
m), 7.04 (1H, d, J=1.0Hz), 7.22-7.50 (5H, m),  
7.55-7.82 (7H, m), 8.14 (1H, d, J=8.4Hz), 8.31  
(1H, d, J=8.4Hz), 8.54 (1H, d, J=7.7Hz), 8.84  
(1H, s)

FAB-MASS :  $m/z = 1285$  ( $M^+ + Na$ )

Example 18

IR (Nujol) : 3351, 1668, 1627, 1540, 1515  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.87 (3H, t, J=6.8Hz), 0.96 (3H,  
d, J=6.7Hz), 1.06 (3H, d, J=5.8Hz), 1.17-1.48  
(4H, m), 1.50-1.95 (5H, m), 2.05-2.70 (8H, m),  
2.70-2.95 (2H, m), 3.05-3.30 (1H, m), 3.60-3.90  
(2H, m), 3.90-4.50 (11H, m), 4.65-5.10 (9H, m),  
5.15 (1H, d, J=3.2Hz), 5.23 (1H, d, J=4.2Hz),  
5.48 (1H, d, J=6.0Hz), 6.67-6.90 (3H, m), 7.03  
(1H, d, J=1.5Hz), 7.15-7.80 (11H, m), 8.00-8.20  
(2H, m), 8.29 (1H, d, J=7.8Hz), 8.84 (1H, s)

FAB-MASS :  $m/z = 1259$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{55}H_{73}N_8O_{21}SNa \cdot 6H_2O$  :

C 50.30, H 6.52, N 8.53

Found : C 50.42, H 6.50, N 8.45

Example 19

IR (Nujol) : 3351, 1668, 1652, 1623, 1540  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.87 (3H, t, J=6.7Hz), 0.96 (3H,  
d, J=6.7Hz), 1.07 (3H, d, J=6.0Hz), 1.25-1.45  
(4H, m), 1.50-2.00 (5H, m), 2.05-2.48 (4H, m),  
2.50-2.75 (2H, m), 3.60-4.50 (13H, m), 4.68-5.25  
(10H, m), 5.27 (1H, d, J=4.5Hz), 5.53 (1H, d,  
J=6.0Hz), 6.67-6.98 (4H, m), 7.05 (1H, d,

195

J=1.0Hz), 7.22-7.58 (5H, m), 7.58-7.90 (7H, m),  
8.16 (1H, d, J=9.0Hz), 8.34 (1H, d, J=8.4Hz),  
8.57 (1H, d, J=7.7Hz), 8.85 (1H, s)

FAB-MASS :  $m/z = 1258$  ( $M^+ + Na$ )

5 Elemental Analysis Calcd. for  $C_{55}H_{71}N_8O_{21}SNa \cdot 5H_2O$  :

C 49.84, H 6.15, N 8.45

Found : C 49.77, H 6.27, N 8.39

Example 20

10 IR (Nujol) : 3353, 1670, 1629, 1540, 1508  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.88 (3H, t, J=6.5Hz), 0.97 (3H,  
d, J=6.8Hz), 1.04 (3H, d, J=5.9Hz), 1.20-1.58  
(8H, m), 1.60-1.96 (5H, m), 2.08-2.60 (6H, m),  
2.70-3.00 (2H, m), 3.00-3.40 (1H, m), 3.60-3.85  
15 (2H, m), 3.85-4.50 (13H, m), 4.50-5.60 (12H, m),  
6.65-6.90 (3H, m), 7.00-7.15 (3H, m), 7.18-7.50  
(4H, m), 7.59 (1H, s), 7.62-7.78 (2H, m), 7.95-  
8.20 (2H, m), 8.30 (1H, d, J=7.7Hz), 8.83 (1H,  
s)

20 FAB-MASS :  $m/z = 1277$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{55}H_{75}N_8O_{22}SNa \cdot 4H_2O$  :

C 49.77, H 6.30, N 8.44

Found : C 49.67, H 6.31, N 8.40

25 Example 21

IR (Nujol) : 3351, 1654, 1623, 1538, 1515  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.87 (3H, t, J=6.7Hz), 0.97 (3H,  
d, J=6.7Hz), 1.08 (3H, d, J=5.9Hz), 1.20-1.58  
(8H, m), 1.66-1.95 (5H, m), 2.10-2.60 (4H, m),  
30 3.09-3.30 (1H, m), 3.58-4.60 (15H, m), 4.69-5.20  
(10H, m), 5.24 (1H, d, J=4.5Hz), 5.51 (1H, d,  
J=6.0Hz), 6.68-6.95 (4H, m), 7.04 (1H, d,  
J=1.0Hz), 7.10-7.73 (7H, m), 7.73-7.90 (2H, m),  
7.98 (1H, d, J=1.9Hz), 8.10 (1H, d, J=8.4Hz),  
35 8.32 (1H, d, J=8.4Hz), 8.50 (1H, d, J=7.7Hz),

196

8.84 (1H, s)

FAB-MASS :  $m/z = 1275$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{55}H_{73}N_8O_{22}SNa \cdot 5H_2O$  :

C 50.38, H 6.38, N 8.55

Found : C 49.98, H 6.37, N 8.41

Example 22

IR (KBr) : 3340, 2931, 1664, 1627, 1531, 1444, 1278,  
1047  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.6Hz$ ), 0.96 (3H,  
d,  $J=6.8Hz$ ), 1.08 (3H, d,  $J=5.9Hz$ ), 1.2-1.4 (6H,  
m), 1.5-1.7 (2H, m), 1.7-2.1 (3H, m), 2.2-2.4  
(3H, m), 2.6-2.7 (3H, m), 3.1-3.2 (1H, m), 3.7-  
4.6 (13H, m), 4.78 (1H, d,  $J=6.0Hz$ ), 4.8-5.1  
(1H, m), 5.09 (1H, d,  $J=5.6Hz$ ), 5.16 (1H, d,  
 $J=3.2Hz$ ), 5.24 (1H, d,  $J=4.4Hz$ ), 5.52 (1H, d,  
 $J=6.0Hz$ ), 6.73 (1H, d,  $J=8.2Hz$ ), 6.83 (2H, d,  
 $J=8.3Hz$ ), 7.05 (1H, s), 7.3-7.5 (5H, m), 7.65  
(2H, d,  $J=8.2Hz$ ), 7.74 (2H, d,  $J=8.4Hz$ ), 7.98  
(2H, d,  $J=8.4Hz$ ), 8.11 (1H, d,  $J=8.4Hz$ ), 8.31  
(1H, d,  $J=8.4Hz$ ), 8.79 (1H, d,  $J=7.7Hz$ ), 8.84  
(1H, s)

FAB-MASS :  $m/z = 1245$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{54}H_{71}N_8O_{21}SNa \cdot 4H_2O$  :

C 50.07, H 6.15, N 8.65

Found : C 50.26, H 6.44, N 8.67

Example 23

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.91 (3H, t,  $J=6.7Hz$ ), 0.96 (3H,  
d,  $J=6.8Hz$ ), 1.05 (3H, d,  $J=5.6Hz$ ), 1.2-1.5 (6H,  
m), 1.6-2.1 (5H, m), 2.1-2.7 (4H, m), 3.0-3.5  
(9H, m), 3.6-4.5 (15H, m), 4.6-5.6 (11H, m),  
6.73 (1H, d,  $J=8.2Hz$ ), 6.8-6.9 (4H, m), 6.95  
(2H, d,  $J=8.6Hz$ ), 7.02 (2H, d,  $J=9.2Hz$ ), 7.04  
(1H, s), 7.2-7.5 (3H, m), 7.82 (2H, d,  $J=8.6Hz$ ),

197



8.06 (1H, d, J=8Hz), 8.25 (1H, d, J=6.7Hz), 8.43  
(1H, d, J=6.7Hz), 8.85 (1H, s)

IR (KBr) : 3350, 1668, 1629, 1510  $\text{cm}^{-1}$

FAB-MASS :  $m/z = 1345$  (M+Na)

5. Elemental Analysis Calcd. for  $\text{C}_{58}\text{H}_{79}\text{N}_{10}\text{O}_{22}\text{SNa}\cdot 6\text{H}_2\text{O}$  :  
C 48.67, H 6.41, N 9.78  
Found : C 48.80, H 6.46, N 9.82

Example 24

- 10 Major product

IR (KBr) : 3350, 1668, 1631, 1047  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.08 (3H,  
d, J=5.7Hz), 1.2-1.6 (10H, m), 1.6-2.4 (8H, m),  
2.5-2.7 (1H, m), 3.18 (1H, m), 3.21 (3H, s),  
3.29 (2H, t, J=6.4Hz), 3.6-3.83 (2H, m), 3.83-  
4.6 (13H, m), 4.7-5.4 (11H, m), 5.51 (1H, d,  
J=5.9Hz), 6.73 (1H, d, J=8.2Hz), 6.83 (1H, d,  
J=8.2Hz), 6.85 (1H, s), 7.04 (2H, d, J=8.4Hz),  
7.06 (1H, s), 7.31 (1H, s), 7.2-7.5 (2H, m),  
7.67 (2H, d, J=8.4Hz), 7.71 (2H, d, J=8.4Hz),  
7.96 (2H, d, J=8.4Hz), 8.06 (1H, d, J=8Hz), 8.25  
(1H, d, J=6.7Hz), 8.74 (1H, d, J=6.7Hz), 8.84  
(1H, s)

FAB-MASS :  $m/z = 1319$  (M+Na)

- 25 Elemental Analysis Calcd. for  $\text{C}_{57}\text{H}_{77}\text{N}_8\text{O}_{23}\text{SNa}\cdot 4\text{H}_2\text{O}$  :  
C 49.99, H 6.26, N 8.18  
Found : C 49.74, H 6.27, N 8.06

Minor product

- 30 IR (KBr) : 3350, 1668, 1631  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.08 (3H,  
d, J=5.7Hz), 1.2-1.6 (6H, m), 1.6-2.1 (7H, m),  
2.1-2.5 (3H, m), 2.5-2.7 (1H, m), 3.18 (1H, m),  
3.6-3.8 (2H, m), 3.8-4.6 (13H, m), 4.6-5.2 (12H,  
m), 5.26 (1H, d, J=4.6Hz), 5.53 (1H, d,

199

J=5.8Hz), 5.6-6.0 (1H, m), 6.73 (1H, d, J=8.2Hz), 6.83 (1H, d, J=8.3Hz), 6.85 (1H, s), 7.04 (2H, d, J=8.5Hz), 7.06 (1H, s), 7.30 (1H, s), 7.2-7.5 (2H, m), 7.68 (2H, d, J=8.5Hz), 7.72 (2H, d, J=8.5Hz), 7.96 (2H, d, J=8.5Hz), 8.06 (1H, d, J=8Hz), 8.25 (1H, d, J=6.7Hz), 8.74 (1H, d, J=6.7Hz), 8.85 (1H, s)

FAB-MASS : m/z = 1287 (M+Na)

Elemental Analysis Calcd. for  $C_{56}H_{73}N_8NaO_{22}S \cdot 7H_2O$  :

C 48.34, H 6.30, N 8.05

Found : C 48.19, H 6.19, N 7.99

#### Example 25

IR (KBr) : 3350, 2935, 2873, 1668, 1629, 1538, 1506, 1438, 1257, 1049  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.9-1.0 (6H, m), 1.08 (3H, d, J=5.7Hz), 1.2-1.6 (4H, m), 1.6-2.0 (5H, m), 2.1-2.4 (3H, m), 2.5-2.6 (1H, m), 3.1-3.2 (1H, m), 3.6-4.6 (15H, m), 4.7-5.2 (10H, m), 5.26 (1H, d, J=4.5Hz), 5.55 (1H, d, J=5.9Hz), 6.7-6.9 (3H, m), 7.0-7.6 (7H, m), 7.85 (2H, d, J=8.6Hz), 7.9-8.2 (4H, m), 8.26 (1H, d, J=7.7Hz), 8.8-9.0 (2H, m)

FAB-MASS : m/z = 1314.3 (M+Na)<sup>+</sup>

Elemental Analysis Calcd. for  $C_{56}H_{70}N_9O_{23}NaS \cdot 7H_2O$  :

C 47.42, H 5.97, N 8.89

Found : C 47.33, H 5.85, N 8.73

#### Example 26

To a solution of The Starting Compound (1 g) and succinimido 4-(4-octyloxyphenyl)piperazine-1-carboxylate (0.45 g) in N,N-dimethylformamide (10 ml) was added 4-dimethylaminopyridine (0.141 g), and stirred for 5 days at 50°C. The reaction mixture was pulverized with ethyl acetate. The precipitate was collected by filtration, and

198

dried under reduced pressure. The powder was dissolved in water, and subjected to column chromatography on ion exchange resin (DOWEX-50WX4) eluting with water. The fractions containing the object compound were combined, and subjected to column chromatography on ODS (YMC-gel-ODS-AM-S-50) eluting with 50% acetonitrile aqueous solution. The fractions containing the object compound were combined, and evaporated under reduced pressure to remove acetonitrile. The residue was lyophilized to give crude The Object Compound (23). The powder of crude The Object Compound (23) was purified by preparative HPLC utilizing a C<sub>18</sub>  $\mu$  Bondapak resin (Waters Associates, Inc.) which was eluted with a solvent system comprised of (acetonitrile-pH 3 phosphate buffer = 40:60) at a flow rate of 80 ml/minute using a Shimadzu LC-8A pump. The column was monitored by a UV detector set at 240 nm. The fractions containing the object compound were combined, and evaporated under reduced pressure to remove acetonitrile. The residue was subjected to column chromatography on ion exchange resin (DOWEX-50WX4) eluting with water. The fractions containing the object compound were combined, and subjected to column chromatography on ODS (YMC-gel-ODS-AM-S-50) eluting with 50% acetonitrile aqueous solution. The fractions containing the object compound were combined, and evaporated under reduced pressure to remove acetonitrile. The residue was lyophilized to give The Object Compound (23) (60 mg).

IR (KBr) : 3347, 1629, 1511, 1245 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.86 (3H, t, J=6.7Hz), 0.95 (3H, d, J=6.8Hz), 1.06 (3H, d, J=5.9Hz), 1.2-1.5 (10H, m), 1.55-1.92 (5H, m), 2.0-2.65 (4H, m), 2.8-3.05 (5H, m), 3.2-4.47 (17H, m), 4.6-5.6 (12H, m), 6.6-7.0 (7H, m), 7.03 (1H, s), 7.2-7.5 (3H, m), 7.9-8.3 (3H, m), 8.84 (1H, s)

FAB-MASS : m/z = 1297 (M<sup>+</sup>+Na)

200

Elemental Analysis Calcd. for  $C_{54}H_{79}N_{10}O_{22}SNa \cdot 6H_2O \cdot CH_3CN$ :  
C 47.22, H 6.65, N 10.82  
Found : C 47.58, H 7.05, N 10.85

5     Example 27

To a suspension of 1-hydroxybenzotriazole (0.53 g) and 2-(4-octyloxyphenoxy)acetic acid (1 g) in dichlormethane (30 ml) was added 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride (WSCD·HCl) (0.886 g), and stirred for 3 hours at ambient temperature. The reaction mixture was added to water. The organic layer was taken, and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give 1-[2-(4-octyloxyphenoxy)acetyl]benzotriazole 3-oxide (892 mg). To a solution of The Starting Compound (1.79 g) and 1-[2-(4-octyloxyphenoxy)acetyl]benzotriazole 3-oxide (892 mg) in N,N-dimethylformamide (18 ml) was added 4-(N,N-dimethylamino)pyridine (0.297 g), and stirred for 12 hours at ambient temperature. The reaction mixture was pulverized with ethyl acetate. The precipitate was collected by filtration, and dried under reduced pressure. The powder was added to water, and subjected to ion-exchange column chromatography on DOWEX-50WX4, and eluted with water. The fractions containing the object compound were combined, and subjected to column chromatograph on ODS (YMC-gel·ODS-AM·S-50), and eluted with 50% methanol aqueous solution. The fractions containing the object compound were combined, and evaporated under reduced pressure to remove methanol. The residue was lyophilized to give The Object Compound (24) (1.75 g).

IR (KBr) : 3350, 1666, 1629, 1228  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.9Hz$ ), 0.95 (3H, d,  $J=6.7Hz$ ), 1.04 (3H, d,  $J=5.7Hz$ ), 1.15-1.5 (10H, m), 1.55-2.0 (5H, m), 2.05-2.5 (4H, m),

201

3.16 (1H, m), 3.72 (2H, m), 3.88 (3H, t,  
J=6.3Hz), 4.41 (2H, s), 3.93-4.6 (11H, m),  
4.69-5.25 (10H, m), 5.28 (1H, d, J=4.3Hz), 5.57  
(1H, d, J=5.7Hz), 6.73 (1H, d, J=8.2Hz), 6.8-7.0  
(5H, m), 7.04 (1H, s), 7.09 (1H, s), 7.3-7.4  
(2H, m), 7.92-8.17 (2H, m), 8.29 (1H, d,  
J=7.5Hz), 8.84 (1H, s)

FAB-MASS :  $m/z = 1243$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{51}H_{73}N_8O_{23}SNa \cdot 4H_2O$  :

C 47.36, H 6.31, N 8.66

Found : C 47.22, H 6.44, N 8.37

The Object Compounds (28) to (31) were obtained  
according to a similar manner to that of Example 27.

#### Example 28

IR (KBr) : 3350, 2933, 1664, 1628, 1446, 1205,  
1045  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.8-1.1 (9H, m), 1.2-2.0 (19H, m),  
2.1-2.3 (3H, m), 3.6-3.8 (4H, m), 3.9-4.4 (13H, m),  
4.6-5.0 (8H, m), 5.07 (1H, d, J=5.6Hz), 5.14 (1H,  
d, J=3.2Hz), 5.23 (1H, d, J=4.3Hz), 5.46 (1H, d,  
J=6.7Hz), 6.7-6.9 (3H, m), 7.04 (1H, s), 7.2-7.5  
(6H, m), 7.8-8.0 (3H, m), 8.05 (1H, d, J=8.4Hz),  
8.2-8.4 (2H, m), 8.83 (1H, s)

FAB-MASS :  $m/z = 1360$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{59}H_{80}N_9O_{23}SNa \cdot 6H_2O$  :

C 48.99, H 6.41, N 8.72

Found : C 48.92, H 6.37, N 8.64

#### Example 29

IR (KBr) : 3350, 2927, 1668, 1627, 1535, 1515, 1452,  
1440, 1286, 1045  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.83 (3H, t, J=6.7Hz), 0.95 (3H,  
d, J=6.7Hz), 1.07 (3H, d, J=5.9Hz), 1.2-1.4

202

(12H, m), 1.6-2.0 (5H, m), 2.1-2.4 (3H, m), 2.6  
(1H, m), 2.82 (2H, t,  $J=7.4\text{Hz}$ ), 3.1-3.2 (1H, m),  
3.6-4.5 (13H, m), 4.7-5.2 (11H, m), 5.4-5.6 (1H,  
m), 6.72 (1H, d,  $J=8.2\text{Hz}$ ), 6.82 (2H, d,  
5  $J=8.1\text{Hz}$ ), 7.03 (1H, s), 7.2-7.4 (3H, m), 7.47  
(1H, d,  $J=8.5\text{Hz}$ ), 7.69 (1H, d,  $J=8.5\text{Hz}$ ), 8.1-8.2  
(2H, m), 8.23 (1H, d,  $J=8.4\text{Hz}$ ), 8.62 (1H, d,  
 $J=7.8\text{Hz}$ ), 8.83 (1H, s)

FAB-MASS :  $m/z = 1251 (M^+ + Na)$

10 Elemental Analysis Calcd. for  $C_{52}H_{73}N_{10}O_{21}SNa \cdot 5H_2O$  :

C 47.34, H 6.34, N 10.61

Found : C 47.30, H 6.45, N 10.45

Example 30

15 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.8\text{Hz}$ ), 0.96 (3H,  
t,  $J=6.7\text{Hz}$ ), 1.05 (3H, t,  $J=5.8\text{Hz}$ ), 1.2-1.5  
(10H, m), 1.6-2.0 (5H, m), 2.2-2.4 (3H, m), 2.5-  
2.6 (1H, m), 3.1-3.2 (1H, m), 3.7-4.5 (15H, m),  
4.7-5.0 (8H, m), 5.10 (1H, d,  $J=5.6\text{Hz}$ ), 5.17  
20 (1H, d,  $J=3.1\text{Hz}$ ), 5.26 (1H, d,  $J=4.5\text{Hz}$ ), 5.52  
(1H, d,  $J=5.8\text{Hz}$ ) 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.8-7.0  
(3H, m), 7.04 (1H, s), 7.2-7.4 (3H, m), 8.0-8.3  
(3H, m), 8.68 (1H, d,  $J=2.3\text{Hz}$ ), 8.7-8.8 (1H, m),  
8.85 (1H, m)

25 FAB-MASS :  $m/z = 1214 (M^+ + Na)$

Elemental Analysis Calcd. for  $C_{49}H_{70}N_9O_{22}SNa \cdot 4H_2O$  :

C 46.55, H 6.22, N 9.97

Found : C 46.29, H 6.18, N 9.71

30 Example 31

IR (Nujol) : 3342, 2210, 1668, 1623  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.7\text{Hz}$ ), 0.97 (3H,  
d,  $J=6.7\text{Hz}$ ), 1.08 (3H, d,  $J=6.7\text{Hz}$ ), 1.20-1.60

(8H, m), 1.60-2.00 (5H, m), 2.05-2.50 (4H, m),  
35 3.05-3.30 (1H, m), 3.60-4.60 (15H, m), 4.65-5.18

203

(10H, m), 5.24 (1H, d,  $J=4.5\text{Hz}$ ), 5.58 (1H, d,  $J=6.0\text{Hz}$ ), 6.68-7.10 (4H, m), 7.15-7.65 (5H, m), 7.80-8.30 (6H, m), 8.84 (1H, s), 9.18 (1H, d,  $J=7.7\text{Hz}$ )

5 FAB-MASS :  $m/z = 1273.5$  ( $M^+ + \text{Na}$ )

Example 32

To a solution of 6-heptyloxy-2-naphthoic acid (0.358 g) and triethylamine (0.174 ml) in N,N-dimethylformamide (10 ml) was added diphenylphosphoryl azide (0.4 ml), and stirred for an hour at ambient temperature. Then, the reaction mixture was stirred for an hour at 100°C. After cooling, to the reaction mixture was added The Starting Compound (1 g) and 4-(N,N-dimethylamino)pyridine (0.140 g), and stirred for 10 hours at ambient temperature. The reaction mixture was pulverized with ethyl acetate. The precipitate was collected by filtration, and dried under reduced pressure. The powder was dissolved in water, and subjected to column chromatography on ion exchange resin (DOWEX-50WX4) eluting with water. The fractions containing the object compound were combined, and subjected to column chromatography on ODS (YMC-gel-ODS-AM-S-50) eluting with 50% acetonitrile aqueous solution. The fractions containing the object compound were combined, and evaporated under reduced pressure to remove acetonitrile. The residue was lyophilized to give The Object Compound (29) (0.832 g).

IR (KBr) : 3350, 1664, 1629, 1546, 1240  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.6\text{Hz}$ ), 0.97 (3H, d,  $J=6.7\text{Hz}$ ), 1.08 (3H, d,  $J=5.9\text{Hz}$ ), 1.2-1.55 (8H, m), 1.55-2.0 (5H, m), 2.1-2.5 (4H, m), 3.18 (1H, m), 3.6-3.8 (3H, m), 3.9-4.5 (13H, m), 4.7-4.95 (3H, m), 5.0-5.3 (7H, m), 5.59 (1H, d,  $J=5.8\text{Hz}$ ), 6.52 (1H, d,  $J=8.1\text{Hz}$ ), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.83 (1H, d,  $J=8.2\text{Hz}$ ), 6.90 (1H, s),

204

7.0-7.15 (3H, m), 7.20 (1H, s), 7.27-7.4 (3H, m), 7.6-7.7 (2H, m), 7.87 (1H, s), 7.95-8.2 (2H, m), 8.69 (1H, s), 8.85 (1H, s)

FAB-MS :  $m/z = 1264$  ( $M^+ + Na$ )

5 Elemental Analysis Calcd. for  $C_{53}H_{72}N_9O_{22}SNa \cdot 5H_2O$  :

C 47.78, H 6.20, N 9.46

Found : C 47.65, H 6.42, N 9.34

10 The Object Compound (33) was obtained according to a similar manner to that of Example 32.

Example 33

IR (KBr) : 3350, 1666, 1629, 1537, 1240  $cm^{-1}$

15 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.7Hz$ ), 0.97 (3H, d,  $J=6.7Hz$ ), 1.09 (3H, d,  $J=5.8Hz$ ), 1.2-1.55 (8H, m), 1.55-2.0 (5H, m), 2.07-2.6 (4H, m), 3.18 (1H, m), 3.6-3.85 (3H, m), 3.9-4.5 (13H, m), 4.7-4.98 (3H, m), 5.0-5.3 (7H, m), 5.57 (1H, d,  $J=5.9Hz$ ), 6.50 (1H, d,  $J=8.1Hz$ ), 6.73 (1H, d,  $J=8.2Hz$ ), 6.82 (1H, dd,  $J=8.2$  and  $1.7Hz$ ), 6.87 (1H, s), 6.97 (2H, d,  $J=8.8Hz$ ), 7.05 (1H, d,  $J=1.7Hz$ ), 7.10 (1H, s), 7.23-7.43 (2H, m), 7.38 (2H, d,  $J=8.8Hz$ ), 7.50 (2H, d,  $J=8.8Hz$ ), 7.52 (2H, d,  $J=8.8Hz$ ), 8.0-8.15 (2H, m), 8.65 (1H, s), 8.84 (1H, s)

25 FAB-MASS :  $m/z = 1290$  ( $M^+ + Na$ )

Elemental Analysis Calcd. for  $C_{55}H_{74}N_9O_{22}SNa \cdot 7H_2O$  :

C 47.38, H 6.36, N 9.04

30 Found : C 47.67, H 6.53, N 9.03

Example 34

35 A solution of The Starting Compound (2.45 g), 3-[4-(4-pentylphenyl)phenyl]propionic acid (0.90 g), 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride (WSCD-HCl) (0.59 g) and triethylamine (0.43 ml) in N,N-

265



dimethylformamide (50 ml) was stirred for 15 hours at ambient temperature. The reaction mixture was diluted with ethyl acetate, and the resultant precipitate was collected by filtration, and washed in turn with ethyl acetate and diisopropyl ether, and dried under reduced pressure. The powder was dissolved in water, and was subjected to column chromatography on ion exchange resin (DOWEX-50WX4 (Na form, 50 ml)) eluting with water. The fractions containing the object compound were combined, and subjected to reversed phase chromatography on ODS (YMC-gel-ODS-AM-S-50, 50 ml) eluting with (water : acetonitrile = 10:0 - 7:3, V/V). The fractions containing the object compound were combined, and evaporated under reduced pressure to remove acetonitrile. The residue was lyophilized to give The Object Compound (31) (1.53 g).

IR (Nujol) : 3351, 2212, 1668, 1627  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.5\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.08 (3H, d,  $J=5.8\text{Hz}$ ), 1.20-1.50 (4H, m), 1.50-2.00 (5H, m), 2.03-2.55 (4H, m), 2.62 (2H, t,  $J=7.5\text{Hz}$ ), 3.17 (1H, t,  $J=8.4\text{Hz}$ ), 3.55-4.57 (15H, m), 4.65-5.13 (9H, m), 5.16 (1H, d,  $J=3.2\text{Hz}$ ), 5.24 (1H, d,  $J=4.5\text{Hz}$ ), 5.58 (1H, d,  $J=5.8\text{Hz}$ ), 6.67-6.90 (3H, m), 6.93-7.10 (2H, m), 7.15-7.50 (4H, m), 7.50-7.90 (6H, m), 8.06 (1H, d,  $J=8.4\text{Hz}$ ), 8.15 (1H, d,  $J=7.7\text{Hz}$ ), 8.84 (1H, s), 9.19 (1H, d,  $J=7.1\text{Hz}$ ).

FAB-MASS :  $m/z = 1255$  ( $M^+ + \text{Na}$ )

Elemental Analysis Calcd. for  $\text{C}_{55}\text{H}_{69}\text{N}_8\text{O}_{21}\text{SNa}\cdot 4\text{H}_2\text{O}$  :

C 50.61, H 5.95, N 8.58

Found : C 50.47, H 6.00, N 8.54

### Example 35

To a suspension of 1-hydroxybenzotriazole (501 mg) and 4-(4-heptylphenyl)benzoic acid (1 g) in dichloromethane (30 ml) was added 1-ethyl-3-(3'-

206

dimethylaminopropyl)carbodiimide hydrochloride (WSCD·HCl) (839 mg), and stirred for 3 hours at ambient temperature. The reaction mixture was added to water. The organic layer was separated, and dried over magnesium sulfate.

5 The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give 1-[4-(4-heptylphenyl)benzoyl]benzotriazole 3-oxide. To a solution of The Starting Compound (2.49 g) and 1-[4-(4-heptylphenyl)benzoyl]benzotriazole 3-oxide in N,N-dimethylformamide (25 ml) was added 4-(N,N-dimethylamino)pyridine (381 mg), and stirred for 12 hours at ambient temperature. The reaction mixture was pulverized with ethyl acetate. The precipitate was collected by filtration, and dried under reduced pressure. 15 The residue was dissolved in water, and subjected to column chromatography on ion exchange resin (DOWEX-50WX4) eluting with water. The fraction containing the object compound were combined, and subjected to column chromatography on ODS (YMC-gel-ODS-AM-S-50) eluting with 20 30% acetonitrile aqueous solution. The fractions containing the object compound were combined, and evaporated under reduced pressure to remove acetonitrile. The residue was lyophilized to give The Object Compound (32) (1.99 g).

25 IR (Nujol) : 3350, 2852, 1749, 1621, 1457, 1376, 1045  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.7\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.08 (3H, d,  $J=5.9\text{Hz}$ ), 1.5-1.7 (2H, m), 1.7-2.2 (3H, m), 2.2-2.5 (3H, m), 2.6-2.8 (3H, m), 3.1-3.2 (1H, m), 3.7-4.6 (13H, m), 4.7-5.2 (8H, m), 5.12 (1H, d,  $J=5.5\text{Hz}$ ), 5.18 (1H, d,  $J=2.9\text{Hz}$ ), 5.27 (1H, d,  $J=4.4\text{Hz}$ ), 5.54 (1H, d,  $J=5.8\text{Hz}$ ), 6.7-6.9 (3H, m), 7.05 (1H, s), 7.2-7.4 (5H, m), 7.65 (2H, d,  $J=8.0\text{Hz}$ ), 7.74 (2H, d,  $J=8.3\text{Hz}$ ), 7.98 (2H, d,  $J=8.3\text{Hz}$ ), 8.11

207

(1H, d, J=8.7Hz), 8.28 (1H, d, J=8.4Hz), 8.78

(1H, d, J=7.3Hz), 8.95 (1H, s)

FAB-MASS : m/z = 1259 (M<sup>+</sup>+Na)

Elemental Analysis Calcd. for C<sub>55</sub>H<sub>73</sub>N<sub>8</sub>O<sub>21</sub>SNa·5H<sub>2</sub>O :

C 49.77, H 6.30, N 8.44

Found : C 49.98, H 6.44, N 8.41

The Object Compounds (36) to (107) were obtained according to a similar manner to that of Example 1.

Example 36

IR (KBr) : 3350, 1675.8, 1629.6, 1515.8 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.86 (6H, d, J=6.6Hz), 0.96 (3H, d, J=6.6Hz), 1.06 (3H, d, J=5.7Hz), 1.1-1.3 (2H, m), 1.4-2.0 (6H, m), 2.0-2.7 (4H, m), 3.1-3.5 (9H, m), 3.66 (2H, t, J=7.3Hz), 3.6-4.5 (13H, m), 4.7-5.6 (12H, m), 6.73 (1H, d, J=8.3Hz), 6.82 (1H, d, J=8.3Hz), 6.8-6.9 (1H, m), 7.02 (2H, d, J=9.0Hz), 7.04 (1H, s), 7.11 (2H, d, J=9.0Hz), 7.2-7.6 (3H, m), 7.50 (2H, d, J=9.0Hz), 7.82 (2H, d, J=9.0Hz), 8.1 (1H, d, J=8.5Hz), 8.28 (1H, d, J=8.5Hz), 8.33 (1H, s), 8.45 (1H, d, J=7.0Hz), 8.84 (1H, s)

FAB-MASS : m/z = 1412 (M+Na)

Elemental Analysis Calcd. for C<sub>60</sub>H<sub>80</sub>N<sub>13</sub>O<sub>22</sub>SNa·9H<sub>2</sub>O :

C 46.42, H 6.36, N 11.73

Found : C 46.64, H 6.43, N 11.62

Example 37

IR (KBr) : 3350, 1668.1, 1629.6, 1268.9 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.85 (3H, t, J=6.6Hz), 0.96 (3H, d, J=6.7Hz), 1.07 (3H, d, J=5.9Hz), 1.2-1.4 (10H, m), 1.4-2.0 (5H, m), 2.0-2.5 (4H, m), 2.61 (2H, t, J=7.2Hz), 3.1-3.3 (1H, m), 3.6-4.5 (13H, m), 4.40 (2H, s), 4.6-5.3 (11H, m), 5.60 (1H, d, J=5.8Hz), 6.73 (1H, d, J=8.2Hz), 6.82 (1H, d, J=8.2Hz), 6.6-

6.9 (1H, m), 7.04 (1H, s), 7.0-7.1 (1H, m), 7.32  
(2H, d, J=8.5Hz), 7.2-7.5 (2H, m), 7.58 (2H, d,  
J=8.5Hz), 7.93 (1H, d, J=7Hz), 8.04 (1H, d,  
J=9.4Hz), 8.41 (1H, s), 8.44 (1H, d, J=9.4Hz), 8.84  
(1H, s)

FAB-MASS : m/z = 1294 (M+Na)

Elemental Analysis Calcd. for  $C_{53}H_{74}N_{11}O_{22}SNa \cdot 7H_2O$  :

C 45.52, H 6.34, N 11.02

Found : C 45.47, H 6.27, N 10.93

### Example 38

#### Major product

IR (KBr) : 3349.7, 1670.1, 1627.6, 1508.1  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.6Hz), 1.06 (3H, d,  
J=5.7Hz), 1.2-1.6 (8H, m), 1.6-2.1 (5H, m), 2.1-2.7  
(4H, m), 3.0-3.2 (5H, m), 3.21 (3H, s), 3.30 (2H,  
t, J=6.5Hz), 3.3-3.5 (4H, m), 3.6-4.5 (15H, m),  
4.7-5.3 (11H, m), 5.49 (1H, d, J=5.9Hz), 6.73 (1H,  
d, J=8.3Hz), 6.8-6.9 (4H, m), 6.95 (2H, d,  
J=9.2Hz), 7.01 (2H, d, J=8.5Hz), 7.04 (1H, s), 7.20  
(1H, s), 7.2-7.5 (2H, m), 7.81 (2H, d, J=8.5Hz),  
8.09 (1H, d, J=8.7Hz), 8.28 (1H, d, J=8.7Hz), 8.45  
(1H, d, J=6.7Hz), 8.84 (1H, s)

FAB-MASS : m/z = 1389 (M+Na)

Elemental Analysis Calcd. for  $C_{60}H_{83}N_{10}O_{23}SNa \cdot 8H_2O$  :

C 47.68, H 6.60, N 9.27

Found : C 47.83, H 6.72, N 9.27

#### Minor product

IR (KBr) : 3338.2, 1646.9, 1511.9  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.06 (3H, d,  
J=5.7Hz), 1.3-1.6 (4H, m), 1.6-2.7 (11H, m), 3.0-  
3.2 (5H, m), 3.3-3.5 (4H, m), 3.6-4.5 (15H, m),  
4.7-5.3 (13H, m), 5.48 (1H, d, J=5.9Hz), 5.7-6.0  
(1H, m), 6.73 (1H, d, J=8.2Hz), 6.8-6.9 (4H, m),

209

6.94 (2H, d, J=9.3Hz), 7.01 (2H, d, J=8.6Hz), 7.04  
(1H, s), 7.2-7.5 (3H, m), 7.81 (2H, d, J=8.6Hz),  
8.06 (1H, d, J=8.7Hz), 8.25 (1H, d, J=8.7Hz), 8.42  
(1H, d, J=6.7Hz), 8.84 (1H, s)

5 FAB-MASS : m/z = 1357 (M+Na)

Elemental Analysis Calcd. for  $C_{59}H_{79}N_{10}O_{22}SNa \cdot 9H_2O$  :

C 47.32, H 6.53, N 9.35

Found : C 47.08, H 6.66, N 9.25

10 Example 39

IR (KBr) : 3350, 1670.1, 1631.5, 1510.0, 1234.2  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.87 (3H, t, J=6.7Hz), 0.96 (3H, d,  
J=6.7Hz), 1.06 (3H, d, J=5.6Hz), 1.2-1.5 (8H, m),  
1.6-2.1 (5H, m), 2.1-2.7 (4H, m), 3.0-3.3 (5H, m),  
-15 3.3-3.5 (4H, m), 3.6-3.8 (2H, m), 3.88 (2H, d,  
J=6.4Hz), 3.8-4.5 (11H, m), 4.7-5.1 (8H, m), 5.10  
(1H, d, J=5.6Hz), 5.16 (1H, d, J=3.1Hz), 5.25 (1H,  
d, J=4.5Hz), 5.48 (1H, d, J=5.9Hz), 6.73 (1H, d,  
J=8.2Hz), 6.8-6.9 (4H, m), 6.94 (2H, d, J=9.3Hz),  
20 7.01 (2H, d, J=8.7Hz), 7.04 (1H, s), 7.2-7.5 (3H,  
m), 7.81 (2H, d, J=8.7Hz), 8.06 (1H, d, J=8Hz),  
8.25 (1H, d, J=6.7Hz), 8.43 (1H, d, J=6.7Hz), 8.85  
(1H, s)

FAB-MASS : m/z = 1359 (M+Na)

25 Elemental Analysis Calcd. for  $C_{59}H_{81}N_{10}O_{22}SNa \cdot 5H_2O$  :

C 49.64, H 6.43, N 9.81

Found : C 49.49, H 6.54, N 9.72

Example 40

30 IR (KBr) : 3355.5, 1670.1, 1627.6, 1510.0 1236.1  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (6H, d, J=6.5Hz), 0.96 (3H, d,  
J=6.7Hz), 1.05 (3H, d, J=5.7Hz), 1.2-1.4 (2H, m),  
1.5-2.1 (6H, m), 2.1-2.7 (4H, m), 3.0-3.6 (9H, m),  
3.6-4.5 (15H, m), 4.5-5.4 (12H, m), 6.73 (1H, d,  
35 J=8.2Hz), 6.8-6.9 (4H, m), 6.96 (2H, d, J=9.6Hz),

210

7.02 (2H, d, J=8.7Hz), 7.05 (1H, s), 7.2-7.5 (3H, m), 7.82 (2H, d, J=8.7Hz), 8.08 (1H, d, J=8Hz), 8.27 (1H, d, J=6.7Hz), 8.46 (1H, d, J=6.7Hz), 8.85 (1H, s)

5 FAB-MASS : m/z = 1345 (M+Na)

Elemental Analysis Calcd. for  $C_{58}H_{79}N_{10}O_{22}SNa \cdot 8H_2O$  :

C 47.47, H 6.52, N 9.54

Found : C 47.47, H 6.54, N 9.51

10 Example 41

IR (KBr) : 3347.8, 1668.1, 1629.6, 1510.0, 1234.2  $cm^{-1}$

15 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (3H, t, J=7.0Hz), 0.96 (3H, d, J=6.7Hz), 1.05 (3H, d, J=5.8Hz), 1.2-1.5 (4H, m), 1.6-2.1 (5H, m), 2.1-2.7 (4H, m), 3.0-3.6 (9H, m), 3.6-3.8 (2H, m), 3.8-4.5 (13H, m), 4.7-5.6 (12H, m), 6.73 (1H, d, J=8.2Hz), 6.8-6.9 (4H, m), 6.96 (2H, d, J=8.7Hz), 7.02 (2H, d, J=9.0Hz), 7.04 (1H, s), 7.2-7.5 (3H, m), 7.82 (2H, d, J=8.7Hz), 8.07 (1H, d, J=8Hz), 8.27 (1H, d, J=6.7Hz), 8.45 (1H, d, J=6.7Hz), 8.85 (1H, s)

20 FAB-MASS : m/z = 1331 (M+Na)

Elemental Analysis Calcd. for  $C_{57}H_{77}N_{10}O_{22}SNa \cdot 6H_2O$  :

C 48.30, H 6.33, N 9.88

Found : C 48.20, H 6.58, N 10.03

25 Example 42

Mixture product

IR (KBr) : 3344, 1670.1, 1631.5  $cm^{-1}$

30 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.08 (3H, d, J=5.9Hz), 1.2-1.5 (8H, m), 1.6-2.1 (7H, m), 2.1-2.7 (4H, m), 3.1-3.3 (1H, m), 3.6-4.5 (15H, m), 4.45 and 4.70 (2H, t, J=7.1Hz), 4.6-5.3 (11H, m), 5.52 (1H, d, J=5.9Hz), 6.73 (1H, d, J=8.2Hz), 6.83 (1H, d, J=8.2Hz), 6.85 (1H, s), 7.03 (2H, d, J=8.6Hz), 7.05 (1H, s), 7.2-7.5 (3H, m), 7.68 (2H, d,

211

J=8.6Hz), 7.71 (2H, d, J=8.4Hz), 7.96 (2H, d,  
J=8.4Hz), 8.12 (1H, d, J=8.5Hz), 8.30 (1H, d,  
J=7.0Hz)

FAB-MASS :  $m/z = 1357$  (M+Na)

5 Elemental Analysis Calcd. for  $C_{57}H_{75}N_{12}O_{22}SNa \cdot 4H_2O$  :  
C 48.64, H 5.94, N 11.94  
Found : C 48.91, H 5.88, N 11.86

Example 43

10 IR (KBr) : 3350, 1666.2, 1651.5  $cm^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.05 (6H, d,  
J=6.3Hz), 1.06 (3H, d, J=5.7Hz), 1.2-1.6 (10H, m),  
1.6-2.1 (7H, m), 2.1-2.7 (6H, m), 2.8-3.0 (2H, m),  
3.0-3.2 (1H, m), 3.4-3.7 (2H, m), 3.6-3.8 (2H, m),  
15 3.8-4.5 (13H, m), 4.7-5.6 (12H, m), 6.73 (1H, d,  
J=8.2Hz), 6.8-7.0 (2H, m), 7.03 (2H, d, J=8.7Hz),  
7.06 (1H, s), 7.2-7.5 (3H, m), 7.67 (2H, d,  
J=8.7Hz), 7.71 (2H, d, J=8.4Hz), 7.96 (2H, d,  
J=8.4Hz), 8.04 (1H, d, J=8.5Hz), 8.31 (1H, d,  
20 J=8.5Hz), 8.73 (1H, d, J=7.0Hz), 8.90 (1H, s)  
FAB-MASS :  $m/z = 1402$  (M+Na)

Example 44

25 IR (KBr pelet) : 3350, 2929, 2856, 1670, 1631, 1510,  
1243, 1045  $cm^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t, J=6.8Hz), 0.96 (3H, d,  
J=6.7Hz), 1.06 (3H, d, J=5.7Hz), 1.6-2.0 (5H, m),  
2.2-2.5 (5H, m), 2.6-2.7 (1H, m), 3.0-3.3 (5H, m),  
3.6-4.5 (19H, m), 4.77 (2H, d, J=5.9Hz), 4.8-5.1  
30 (6H, m), 5.10 (1H, d, J=5.6Hz), 5.17 (1H, d,  
J=3.1Hz), 5.25 (1H, d, J=4.5Hz), 5.50 (1H, d,  
J=5.8Hz), 6.7-7.0 (8H, m), 7.04 (1H, s), 7.2-7.4  
(3H, m), 8.0-8.2 (2H, m), 8.26 (1H, d, J=8.0Hz),  
8.55 (1H, d, J=7.3Hz), 8.67 (1H, d, J=1.2Hz), 8.85  
35 (1H, s)

212

FAB-MASS :  $m/z = 1374.3$  ( $M+Na^+$ )

Elemental Analysis Calcd. for  $C_{59}H_{82}N_{11}O_{22}NaS \cdot 5.5H_2O$  :

C 48.82, H 6.46, N 10.61

Found : C 48.89, H 6.74, N 10.50

5

Example 45

IR (KBr) : 3350, 2935, 1668, 1623, 1538, 1257, 1174,  
1047  $cm^{-1}$

10 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.8-1.1 (6H, m), 1.09 (3H, d,  
J=5.7Hz), 1.2-1.6 (6H, m), 1.7-2.1 (5H, m), 2.2-2.4  
(3H, m), 2.5-2.6 (1H, m), 3.6-3.8 (2H, m), 3.8-4.6  
(14H, m), 4.8-5.2 (7H, m), 5.18 (1H, d, J=3.1Hz),  
5.26 (1H, d, J=4.5Hz), 5.54 (1H, d, J=5.8Hz), 6.7-  
15 7.5 (9H, m), 7.82 (1H, d, J=8.5Hz), 7.96 (1H, d,  
J=8.7Hz), 8.1-8.4 (5H, m), 8.8-9.0 (2H, m)

FAB-MASS :  $m/z = 1302.6$  ( $M+Na^+$ )

Elemental Analysis Calcd. for  $C_{55}H_{70}N_9O_{23}Na \cdot 6H_2O$  :

C 47.58, H 5.95, N 9.08

Found : C 47.46, H 6.04, N 9.05

20

Example 46

IR (KBr) : 3355, 2958, 1670, 1627, 1521, 1247,  
1047  $cm^{-1}$

25 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.9-1.0 (6H, m), 1.08 (3H, d,  
J=5.6Hz), 1.4-1.6 (2H, m), 1.7-2.1 (5H, m), 2.1-2.4  
(3H, m), 2.5-2.6 (1H, m), 3.1-3.3 (1H, m), 3.7-3.8  
(2H, m), 3.9-4.6 (13H, m), 4.8-5.1 (8H, m), 5.11  
(1H, d, J=5.6Hz), 5.17 (1H, d, J=3.1Hz), 5.26 (1H,  
d, J=4.5Hz), 5.54 (1H, d, J=5.9Hz), 6.7-6.9 (3H,  
30 m), 7.0-7.2 (3H, m), 7.3-7.5 (3H, m), 7.7-7.9 (8H,  
m), 8.02 (2H, d, J=8.4Hz), 8.08 (1H, d, J=8.4Hz),  
8.32 (1H, d, J=7.7Hz), 8.81 (1H, d, J=7.0Hz), 8.85  
(1H, s)

FAB-MASS :  $m/z = 1309.3$  ( $M+Na$ )<sup>+</sup>

35

Elemental Analysis Calcd. for  $C_{58}H_{71}N_8O_{22}NaS \cdot 6H_2O$  :

213



C 49.92, H 6.00, N 8.03

Found : C 49.92, H 5.97, N 8.03

Example 47

5 IR (KBr) : 3350, 2933, 1668, 1629, 1517, 1249,  
1045  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.7\text{Hz}$ ), 0.96 (3H, d,  
 $J=6.7\text{Hz}$ ), 1.08 (3H, d,  $J=5.8\text{Hz}$ ), 1.7-2.7 (8H, m),  
3.1-3.3 (1H, m), 3.6-4.5 (16H, m), 4.7-5.2 (8H, m),  
10 5.18 (1H, d,  $J=3.1\text{Hz}$ ), 5.27 (1H, d,  $J=4.5\text{Hz}$ ), 5.56  
(1H, d,  $J=5.8\text{Hz}$ ), 6.7-7.0 (3H, m), 7.0-7.2 (3H, m),  
7.2-7.5 (3H, m), 8.0-8.4 (6H, m), 8.85 (1H, s),  
8.96 (1H, d,  $J=7.0\text{Hz}$ ), 9.07 (1H, s)

FAB-MASS :  $m/z = 1276.6$  ( $M+\text{Na}^+$ )

15 Elemental Analysis Calcd. for  $\text{C}_{54}\text{H}_{72}\text{N}_9\text{O}_{22}\text{NaS}\cdot 5\text{H}_2\text{O}$  :

C 48.25, H 6.15, N 9.38

Found : C 48.10, H 6.14, N 9.30

Example 48

IR (KBr) : 3350, 2931, 1668, 1629, 1537, 1049  $\text{cm}^{-1}$

20 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.9\text{Hz}$ ), 0.9-1.5  
(16H, m), 1.6-2.4 (8H, m), 2.5-2.7 (1H, m), 3.1-3.3  
(1H, m), 3.5-5.6 (25H, m), 6.6-7.4 (8H, m), 7.8-8.4  
(6H, m), 8.7-9.0 (2H, m), 9.00 (1H, d,  $J=2.4\text{Hz}$ )

FAB-MASS :  $m/z = 1331.4$  ( $M+\text{Na}^+$ )

25 Elemental Analysis Calcd. for  $\text{C}_{56}\text{H}_{73}\text{N}_{10}\text{O}_{23}\text{NaS}\cdot 8\text{H}_2\text{O}$  :

C 46.28, H 6.17, N 9.64

Found : C 46.50, H 6.27, N 9.65

Example 49

30 IR (KBr pelet) : 3300, 2931, 1668, 1650, 1629, 1538,  
1515, 1268, 1049  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.6\text{Hz}$ ), 0.97 (3H, d,  
 $J=6.7\text{Hz}$ ), 1.10 (3H, d,  $J=5.6\text{Hz}$ ), 1.2-1.4 (6H, m),  
1.5-1.7 (2H, m), 1.7-2.1 (3H, m), 2.1-2.4 (3H, m),  
35 2.6-2.7 (3H, m), 3.1-3.2 (1H, m), 3.7-3.9 (2H, m),

214

3.9-4.5 (12H, m), 4.8-5.1 (7H, m), 5.11 (1H, d, J=5.5Hz), 5.18 (1H, d, J=3.1Hz), 5.27 (1H, d, J=4.5Hz), 5.55 (1H, d, J=5.8Hz), 6.7-7.0 (3H, m), 7.06 (1H, s), 7.3-7.5 (5H, m), 7.72 (2H, d, J=8.2Hz), 7.9-8.2 (5H, m), 8.3-8.4 (4H, m), 8.9-9.0 (2H, m)

FAB-MASS :  $m/z = 1260.5$  ( $M+Na^+$ )

Elemental Analysis Calcd. for  $C_{61}H_{74}N_9O_{22}SNa \cdot 6H_2O$  :

C 50.58, H 5.98, N 8.70

Found : C 50.34, H 6.16, N 8.55

Example 50

IR (KBr) : 3369, 2958, 2935, 1670, 1629, 1525, 1473, 1247, 1047  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.95 (3H, t, J=7.3Hz), 0.97 (3H, d, J=6.7Hz), 1.09 (3H, d, J=5.7Hz), 1.3-1.6 (2H, m), 1.7-2.1 (5H, m), 2.1-2.4 (3H, m), 2.5-2.6 (1H, m), 3.1-3.3 (1H, m), 3.7-4.6 (15H, m), 4.7-5.1 (8H, m), 5.10 (1H, d, J=5.6Hz), 5.18 (1H, d, J=3.1Hz), 5.26 (1H, d, J=4.4Hz), 5.56 (1H, d, J=5.7Hz), 6.7-7.0 (3H, m), 7.1-7.2 (3H, m), 7.2-7.4 (3H, m), 7.70 (2H, d, J=8.6Hz), 7.78 (2H, d, J=8.4Hz), 8.1-8.4 (6H, m), 8.85 (1H, s), 8.99 (1H, d, J=7.0Hz), 9.13 (1H, d, J=1.6Hz)

FAB-MASS :  $m/z = 1310.1$  ( $M+Na$ )<sup>+</sup>

Elemental Analysis Calcd. for  $C_{57}H_{70}N_9O_{22}NaS \cdot 7H_2O$  :

C 47.20, H 6.12, N 8.69

Found : C 47.42, H 6.19, N 8.92

Example 51

IR (KBr) : 3351, 2937, 2875, 1670, 1627, 1533, 1245, 1047  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.08 (3H, d, J=5.7Hz), 1.5-1.7 (2H, m), 1.7-2.1 (7H, m), 2.1-2.4 (3H, m), 2.5-2.6 (1H, m), 3.1-3.2 (1H, m), 3.7-

215

3.8 (2H, m), 3.9-4.6 (15H, m), 4.7-4.9 (3H, m),  
5.0-5.1 (5H, m), 5.10 (1H, d, J=5.6Hz), 5.17 (1H,  
d, J=3.1Hz), 5.26 (1H, d, J=4.5Hz), 5.52 (1H, d,  
J=5.9Hz), 6.7-7.1 (9H, m), 7.2-7.5 (5H, m), 7.68  
(2H, d, J=8.2Hz), 7.72 (2H, d, J=6.7Hz), 7.96 (2H,  
d, J=8.2Hz), 8.06 (1H, d, J=8.4Hz), 8.28 (1H, d,  
J=7.7Hz), 8.76 (1H, d, J=7.0Hz), 8.85 (1H, s)

FAB-MASS :  $m/z = 1339.5$  ( $M+Na^+$ )

Elemental Analysis Calcd. for  $C_{59}H_{73}N_8O_{23}NaS \cdot 7H_2O$  :

C 49.09, H 6.08, N 7.76

Found : C 49.04, H 6.08, N 7.82

#### Example 52

IR (KBr) : 3350, 2954, 2937, 1670, 1631, 1440, 1257,  
1047  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (3H, t, J=6.8Hz), 0.97 (3H, d,  
J=6.7Hz), 1.09 (2H, d, J=5.8Hz), 1.2-1.5 (6H, m),  
1.7-2.1 (5H, m), 2.1-2.4 (3H, m), 2.5-2.6 (1H, m),  
3.1-3.2 (1H, m), 3.7-4.6 (15H, m), 4.7-5.3 (11H,  
m), 5.5-5.6 (1H, m), 6.7-6.9 (1H, m), 7.0-7.5 (6H,  
m), 8.0-8.4 (8H, m), 8.85 (1H, s), 8.96 (1H, d,  
J=7.0Hz)

APCI-MASS :  $m/z = 1329.0$  ( $M+Na$ ) $^+$

Elemental Analysis Calcd. for  $C_{56}H_{71}N_{10}O_{23}NaS \cdot 6H_2O$  :

C 47.52, H 5.91, N 9.90

Found : C 47.42, H 6.05, N 9.90

#### Example 53

IR (KBr) : 3350, 2952, 1666, 1629, 1537, 1519,  
1255  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (3H, t, J=6.7Hz), 0.96 (3H, d,  
J=6.4Hz), 1.08 (3H, d, J=5.6Hz), 1.7-2.4 (8H, m),  
2.5-2.6 (1H, m), 3.7-4.5 (15H, m), 4.7-5.1 (8H, m),  
5.11 (1H, d, J=5.5Hz), 5.17 (1H, d, J=3.1Hz), 5.26  
(1H, d, J=3.1Hz), 5.56 (1H, d, J=5.7Hz), 6.73 (1H,

216

d, J=8.2Hz), 6.7-7.0 (2H, m), 7.05 (1H, s), 7.13  
(2H, d, J=8.7Hz), 7.2-7.5 (3H, m), 7.97 (2H, d,  
J=8.7Hz), 8.1-8.4 (6H, m), 8.85 (1H, s), 8.92 (1H,  
d, J=7.0Hz)

5 FAB-MASS :  $m/z = 1345.3$  (M+Na)<sup>+</sup>

Elemental Analysis Calcd. for

$C_{56}H_{71}N_{10}O_{22}S_2Na \cdot 8H_2O$  :

C 45.84, H 5.98, N 9.55

Found : C 45.87, H 6.07, N 9.55

10

Example 54

IR (KBr pelet) : 3350, 2931, 1670, 1652, 1628, 1442,  
1247, 1047  $cm^{-1}$

15 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t, J=6.6Hz), 0.97 (3H, d,  
J=6.8Hz), 1.12 (3H, d, J=6.8Hz), 1.2-1.5 (10H, m),  
1.7-2.0 (5H, m), 2.2-2.4 (3H, m), 2.5-2.6 (1H, m),  
3.1-3.2 (1H, m), 3.72 (2H, br), 3.8-4.5 (17H, m),  
4.7-5.2 (9H, m), 5.26 (1H, d, J=4.6Hz), 5.57 (1H,  
20 d, J=5.7Hz), 6.7-7.1 (7H, m), 7.3-7.5 (3H, m), 7.66  
(2H, d, J=8.7Hz), 8.10 (1H, d, J=7.6Hz), 8.17 (1H,  
d, J=7.6Hz), 8.76 (1H, d, J=7.0Hz), 8.85 (1H, s)

FAB-MASS :  $m/z = 1293$  (M+Na<sup>+</sup>)

Elemental Analysis Calcd. for  $C_{54}H_{75}N_{10}O_{22}NaS \cdot 7H_2O$  :

C 46.41, H 6.42, N 10.02

25 Found : C 46.51, H 6.43, N 9.95

Example 55

IR (KBr) : 3345, 2937, 1650, 1511, 1249, 1047  $cm^{-1}$

30 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.91 (3H, t, J=7.0Hz), 0.96 (3H, t,  
J=7.8Hz), 1.09 (3H, d, J=6.8Hz), 1.3-1.5 (4H, m),  
1.6-2.1 (5H, m), 2.1-2.5 (3H, m), 2.5-2.6 (1H, m),  
3.1-3.3 (1H, m), 3.7-3.9 (2H, m), 3.9-4.6 (13H, m),  
4.79 (2H, d, J=5.9Hz), 4.8-4.9 (1H, m), 4.9-5.2  
(5H, m), 5.10 (1H, d, J=5.9Hz), 5.17 (1H, d,  
35 J=3.1Hz), 5.25 (1H, d, J=4.6Hz), 5.53 (1H, d,

217

J=5.9Hz), 6.7-7.0 (3H, m), 7.0-7.2 (3H, m), 7.19  
(1H, s), 7.3-7.5 (3H, m), 7.7-8.1 (6H, m), 8.08  
(1H, d, J=10.0Hz), 8.26 (1H, d, J=8.8Hz), 8.77 (1H,  
m), 8.85 (1H, s), 13.32 (1H, s)

5 FAB-MASS :  $m/z = 1314.0$  (M+Na)<sup>+</sup>

Elemental Analysis Calcd. for  $C_{56}H_{71}N_{10}O_{22}SNa \cdot 8H_2O$  :

C 46.86, H 6.11, N 9.76

Found : C 46.93, H 5.87, N 9.74

10 Example 56

IR (KBr) : 3350, 2958, 2935, 2873, 1666, 1629, 1247,  
1045  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.9-1.1 (6H, m), 1.08 (3H, d,  
J=6.0Hz), 1.4-1.6 (2H, m), 1.6-2.1 (5H, m), 2.1-2.4  
15 (3H, m), 2.5-2.6 (1H, m), 3.1-3.3 (1H, m), 3.6-4.5  
(15H, m), 4.7-5.1 (8H, m), 5.10 (1H, d, J=5.5Hz),  
5.17 (1H, d, J=2.9Hz), 5.25 (1H, d, J=4.5Hz), 5.55  
(1H, d, J=5.7Hz), 6.7-6.9 (3H, m), 7.0-7.5 (8H, m),  
7.68 (2H, d, J=8.9Hz), 7.73 (2H, d, J=8.3Hz), 8.01  
20 (2H, d, J=8.3Hz), 8.10 (1H, d, J=8.4Hz), 8.26 (1H,  
d, J=7.7Hz), 8.8-9.0 (2H, m)

FAB-MASS :  $m/z = 1299.5$  (M+Na)<sup>+</sup>

Elemental Analysis Calcd. for  $C_{56}H_{69}N_8O_{23}NaS \cdot 6H_2O$  :

C 48.55, H 5.89, N 8.09

25 Found : C 48.52, H 5.94, N 8.07

Example 57

IR (KBr) : 3355.5, 1662.3, 1629.6, 1267.0  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.88 (3H, t, J=6.8Hz), 0.93 (3H, d,  
30 J=8.4Hz), 0.97 (3H, d, J=6.7Hz), 1.2-1.5 (4H, m),  
1.5-1.95 (5H, m), 2.1-2.45 (4H, m), 2.5-2.7 (4H,  
m), 3.17 (1H, m), 3.55-4.45 (14H, m), 4.6-5.3 (13H,  
m), 5.56 (1H, d, J=5.6Hz), 6.72 (1H, d, J=8.1Hz),  
6.75 (1H, s), 6.77 (1H, d, J=8.1Hz), 7.04 (1H, s),  
35 7.10 (1H, s), 7.2-7.45 (10H, m), 7.53 (4H, d,

218

J=6.6Hz), 7.85 (1H, d, J=7Hz), 7.92 (1H, d, J=7Hz),  
8.05 (1H, d, J=7Hz), 8.22 (1H, d, J=7Hz), 8.84 (1H,  
s)

FAB-MASS : m/z = 1408 (M+Na)

5

Example 58

IR (KBr) : 3347.8, 1664.3, 1631.5, 1245.8 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.86 (3H, t, J=6.6Hz), 0.96 (3H, d,  
J=6.6Hz), 1.04 (3H, d, J=5.7Hz), 1.15-2.6 (21H,  
m), 3.16 (1H, m), 3.5-4.5 (16H, m), 4.6-5.4 (13H,  
m), 5.47 (1H, d, J=5.7Hz), 6.73 (1H, d, J=8.2Hz)  
6.78-6.85 (4H, m), 7.05 (1H, s), 7.10 (1H, s), 7.18  
(2H, d, J=8.6Hz), 7.25-7.45 (6H, m), 7.72 (1H, d,  
J=7Hz), 7.91 (1H, d, J=7Hz), 8.05 (1H, d, J=9.3Hz),  
8.20 (1H, d, J=7Hz), 8.85 (1H, s)

FAB-MASS : m/z = 1390 (M+Na)

Elemental Analysis Calcd. for C<sub>60</sub>H<sub>82</sub>N<sub>9</sub>O<sub>24</sub>SNa·5H<sub>2</sub>O :

C 49.41, H 6.36, N 8.64

Found : C 49.77, H 6.71, N 8.71

Example 59

IR (KBr) : 3353.6, 1670.1, 1627.6, 1247.7 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.86 (3H, t, J=6.5Hz), 0.97 (3H, d,  
J=6.8Hz), 1.01 (3H, d, J=5.4Hz), 1.1-1.55 (12H, m),  
1.55-1.95 (5H, m), 2.05-4.7 (4H, m), 3.16 (1H, m),  
3.5-4.5 (16H, m), 4.6-5.3 (13H, m), 5.55 (1H, d,  
J=5.6Hz), 6.7-6.9 (5H, m), 7.05 (1H, s), 7.1 (1H,  
s), 7.15 (1H, d, J=8.5Hz), 7.25-7.5 (6H, m), 7.73  
(1H, d, J=8.4Hz), 7.92 (1H, d, J=7Hz), 8.08 (1H, d,  
J=8.4Hz), 8.18 (1H, d, J=7Hz), 8.84 (1H, s)

FAB-MASS : m/z = 1390 (M+Na)

Example 60

NMR (DMSO-d<sub>6</sub>, δ) : 0.85 (3H, t, J=6.6Hz), 0.96 (3H, d,  
J=6.6Hz), 1.05 (3H, d, J=5.6Hz), 1.1-1.5 (22H, m),

219

1.5-2.5 (9H, m), 2.5-3.5 (4H, m), 3.5-4.45 (14H, m), 4.45-5.45 (12H, m), 6.72 (1H, d, J=8.2Hz), 6.79 (1H, s), 6.81 (1H, d, J=8.2Hz), 7.04 (1H, s), 7.05-7.5 (8H, m), 7.9-8.3 (3H, m), 8.84 (1H, s)

5 FAB-MASS : m/z = 1325 (M+Na)

Elemental Analysis Calcd. for  $C_{58}H_{89}N_8O_{22}SNa \cdot 6H_2O$  :

C 49.35, H 7.14, N 7.94

Found : C 49.33, H 7.04, N 7.87

10 Example 61

IR (KBr) : 3400, 1668.1, 1629.6, 1270.9  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.8Hz), 1.06 (3H, d, J=5.7Hz), 1.1-2.0 (33H, m), 2.1-2.5 (4H, m), 3.20 (3H, s), 3.28 (2H, t, J=6.5Hz), 3.1-3.3 (1H, m), 15 3.6-4.45 (14H, m), 4.6-5.3 (13H, m), 5.49 (1H, d, J=6.1Hz), 6.70 (1H, s), 6.72 (1H, d, J=8.2Hz), 6.80 (1H, d, J=8.2Hz), 7.03 (1H, s), 7.0-7.1 (1H, m), 7.15 (1H, s), 7.2-7.45 (6H, m), 8.0-8.3 (3H, m), 8.83 (1H, s)

20 FAB-MASS : m/z = 1426 (M+Na)

Elemental Analysis Calcd. for  $C_{62}H_{94}N_9O_{24}SNa \cdot 5H_2O$  :

C 49.82, H 7.01, N 8.43

Found : C 49.86, H 7.31, N 8.40

25 Example 62

IR (KBr) : 3355.5, 1668.1, 1629.6, 1274.7  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.85 (3H, t, J=6.5Hz), 0.96 (3H, d, J=6.7Hz), 1.04 (3H, d, J=5.9Hz), 1.1-2.6 (34H, m), 3.2 (1H, m), 3.6-4.55 (14H, m), 4.7-5.3 (11H, m), 30 5.47 (1H, d, J=5.9Hz), 6.72 (1H, d, J=8.1Hz), 6.79 (1H, s), 6.81 (1H, d, J=8.1Hz), 7.05 (1H, s), 7.11 (1H, s), 7.2-7.5 (2H, m), 8.0-8.15 (2H, m), 8.20 (1H, d, J=8.0Hz), 8.84 (1H, s)

FAB-MASS : m/z = 1235 (M+Na)

35 Elemental Analysis Calcd. for  $C_{51}H_{81}N_8O_{22}SNa \cdot 7H_2O$  :

220

C 45.73, H 7.15, N 8.37

Found : C 45.55, H 7.24, N 8.23

Example 63

5 IR (KBr) : 3353.6, 1664.3, 1627.6  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.6\text{Hz}$ ), 0.95 (3H, d,  $J=6.7\text{Hz}$ ), 1.04 (3H, d,  $J=5.7\text{Hz}$ ), 1.2-2.7 (30H, m), 3.16 (1H, m), 3.6-4.5 (13H, m), 4.7-5.3 (11H, m), 5.51 (1H, d,  $J=6.0\text{Hz}$ ), 5.74 (1H, s), 6.72 (1H, d,  $J=8.2\text{Hz}$ ), 6.75 (1H, s), 6.77 (1H, d,  $J=8.2\text{Hz}$ ), 7.05 (1H, s), 7.2-7.5 (3H, m), 8.0-8.3 (3H, m), 8.85 (1H, s)

FAB-MASS :  $m/z$  = 1204 (M+Na)

Elemental Analysis Calcd. for  $\text{C}_{50}\text{H}_{77}\text{N}_8\text{O}_{21}\text{SNa}\cdot 5\text{H}_2\text{O}$  :

15 C 47.24, H 6.90, N 8.81

Found : C 46.98, H 7.12, N 8.72

Example 64

Major product

20 IR (KBr) : 3400, 1675.8, 1631.5, 1511.9, 1234.2  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.6\text{Hz}$ ), 1.05 (3H, d,  $J=5.8\text{Hz}$ ), 1.2-1.6 (10H, m), 1.6-2.1 (5H, m), 2.1-2.7 (4H, m), 3.05-3.2 (4H, m), 3.20 (3H, s), 3.29 (2H, t,  $J=6.4\text{Hz}$ ), 3.3-3.5 (5H, m), 3.6-4.5 (15H, m), 4.7-5.3 (11H, m), 5.50 (1H, d,  $J=5.8\text{Hz}$ ), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.8-7.1 (9H, m), 7.2-7.5 (3H, m), 7.81 (2H, d,  $J=8.6\text{Hz}$ ), 8.08 (1H, d,  $J=8.2\text{Hz}$ ), 8.24 (1H, d,  $J=7\text{Hz}$ ), 8.44 (1H, d,  $J=7\text{Hz}$ ), 8.84 (1H, s)

FAB-MASS :  $m/z$  = 1403 (M+Na)

30 Elemental Analysis Calcd. for  $\text{C}_{61}\text{H}_{85}\text{N}_{10}\text{O}_{23}\text{SNa}\cdot 9\text{H}_2\text{O}$  :

C 47.47, H 6.73, N 9.07

Found : C 47.43, H 7.06, N 9.03

Minor product

35 IR (KBr) : 3350, 1668.1, 1631.5, 1511.9, 1234.2  $\text{cm}^{-1}$

221



NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.96 (3H, d, J=6.6Hz), 1.07 (3H, d, J=5.8Hz), 1.2-1.5 (6H, m), 1.55-2.1 (7H, m), 2.1-2.65 (4H, m), 3.0-3.6 (9H, m), 3.7-4.5 (15H, m), 4.7-5.6 (14H, m), 5.7-6.0 (1H, m), 6.72 (1H, d, J=8.0Hz), 6.75-7.1 (9H, m), 7.25-7.5 (3H, m), 7.81 (2H, d, J=8.3Hz), 8.08 (1H, d, J=8.2Hz), 8.25 (1H, d, J=7Hz), 8.45 (1H, d, J=7Hz), 8.85 (1H, s)

FAB-MASS : m/z = 1371 (M+Na)

Elemental Analysis Calcd. for C<sub>60</sub>H<sub>81</sub>N<sub>10</sub>O<sub>22</sub>SNa·8H<sub>2</sub>O :

C 48.25, H 6.55, N 9.38

Found : C 48.10, H 6.81, N 9.40

#### Example 65

IR (KBr) : 3450, 1668.1, 1635.3 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.88 (3H, t, J=6.5Hz), 0.96 (3H, d, J=6.7Hz), 1.06 (3H, d, J=6Hz), 1.2-1.5 (6H, m), 1.6-2.1 (5H, m), 2.1-2.7 (4H, m), 3.1-3.4 (9H, m), 3.6-4.5 (15H, m), 4.7-5.3 (11H, m), 5.49 (1H, d, J=5.8Hz), 6.73 (1H, d, J=8.2Hz), 6.8-7.0 (2H, m), 6.83 (2H, d, J=9.0Hz), 6.94 (2H, d, J=9.0Hz), 7.04 (1H, s), 7.12 (1H, t, J=8.4Hz), 7.2-7.5 (3H, m), 7.65-7.8 (2H, m), 8.09 (1H, d, J=8.4Hz), 8.25 (1H, d, J=7Hz), 8.63 (1H, d, J=7Hz), 8.84 (1H, s)

FAB-MASS : m/z = 1363 (M+Na)

Elemental Analysis Calcd. for C<sub>58</sub>H<sub>78</sub>FN<sub>10</sub>O<sub>22</sub>SNa·5H<sub>2</sub>O :

C 48.67, H 6.20, N 9.79

Found : C 48.83, H 6.15, N 9.74

#### Example 66

IR (KBr) : 3400, 1668.1, 1635.3, 1510.0, 1240.0 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.88 (3H, t, J=6.6Hz), 1.2-1.5 (6H, m), 1.5-2.05 (5H, m), 2.1-2.65 (4H, m), 3.1-3.3 (9H, m), 3.6-4.5 (15H, m), 4.7-5.3 (11H, m), 5.51 (1H, d, J=5.8Hz), 6.73 (1H, d, J=8.2Hz), 6.8-6.9 (4H, m), 6.94 (2H, d, J=9.2Hz), 7.04 (1H, s), 7.24

220

(1H, d, J=8.5Hz), 7.15-7.5 (3H, m), 7.86 (1H, dd, J=8.6 and 2.1Hz), 8.02 (1H, d, J=2.1Hz), 8.04 (1H, d, J=8.4Hz), 8.23 (1H, d, J=7Hz), 8.70 (1H, d, J=7Hz), 8.84 (1H, s)

5 FAB-MASS : m/z = 1379 (M+Na)

Elemental Analysis Calcd. for  $C_{53}H_{78}ClN_{10}O_{22}SNa \cdot 6H_2O$  :

C 47.52, H 6.19, N 9.55

Found : C 47.78, H 6.23, N 9.55

10 Example 67

IR (KBr) : 3400, 1670  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.05 (3H, d, J=5.7Hz), 1.4-2.65 (17H, m), 2.65-3.6 (8H, m), 3.6-4.5 (15H, m), 4.6-5.3 (11H, m), 5.44 (1H, d, J=6.0Hz), 6.73 (1H, d, J=8.2Hz), 6.81 (1H, s), 6.83 (1H, d, J=8.2Hz), 6.98 (2H, d, J=8.9Hz), 7.05 (1H, s), 7.2-7.5 (3H, m), 7.80 (2H, d, J=8.9Hz), 8.05 (1H, d, J=8.4Hz), 8.26 (1H, d, J=7Hz), 8.39 (1H, d, J=7Hz), 8.84 (1H, s)

20 FAB-MASS : m/z = 1229 (M+Na)

Elemental Analysis Calcd. for  $C_{52}H_{74}N_{10}O_{21}S \cdot 5H_2O$  :

C 48.14, H 6.53, N 10.80

Found : C 48.29, H 6.33, N 10.95

25 Example 68

IR (KBr) : 3400, 1652.7, 1635.3, 1511.9, 1241.9  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.88 (3H, t, J=6.6Hz), 0.97 (3H, d, J=6.7Hz), 1.09 (3H, d, J=5.7Hz), 1.2-1.5 (6H, m), 1.6-2.0 (5H, m), 2.1-2.6 (4H, m), 3.0-3.3 (5H, m), 3.6-4.6 (19H, m), 4.7-5.3 (11H, m), 5.53 (1H, d, J=5.6Hz), 6.73 (1H, d, J=8.2Hz), 6.75-7.0 (2H, m), 6.83 (2H, d, J=9.2Hz), 6.95 (2H, d, J=9.2Hz), 7.05 (1H, s), 7.12 (1H, s), 7.25-7.5 (2H, m), 7.42 (1H, d, J=9.5Hz), 7.84 (1H, d, J=9.5Hz), 7.9-8.1 (2H, m), 8.71 (1H, d, J=7Hz), 8.84 (1H, s)

FAB-MASS :  $m/z = 1347$  (M+Na)

Elemental Analysis Calcd. for  $C_{56}H_{77}N_{12}O_{22}SNa \cdot 7H_2O$  :

C 46.34, H 6.32, N 11.58

Found : C 46.38, H 6.18, N 11.36

5

Example 69

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.6$ Hz), 0.97 (3H, d,  $J=6.7$ Hz), 1.08 (3H, d,  $J=5.8$ Hz), 1.2-1.5 (6H, m), 1.6-2.05 (5H, m), 2.1-2.6 (4H, m), 3.0-3.3 (5H, m), 3.4-3.55 (4H, m), 3.7-4.6 (15H, m), 4.7-5.3 (11H, m), 5.52 (1H, d,  $J=5.8$ Hz), 6.73 (1H, d,  $J=8.1$ Hz), 6.8-6.95 (2H, m), 6.83 (2H, d,  $J=9.3$ Hz), 6.95 (2H, d,  $J=9.3$ Hz) 7.05 (1H, s), 7.14 (1H, s), 7.3-7.6 (3H, m), 7.84 (1H, d,  $J=8.6$ Hz), 7.95-8.1 (2H, m), 8.40 (1H, s), 8.42 (1H, d,  $J=7$ Hz), 8.84 (1H, s)

FAB-MASS :  $m/z = 1346$  (M+Na)

Elemental Analysis Calcd. for  $C_{57}H_{78}N_{11}O_{22}SNa \cdot 5H_2O$  :

C 48.40, H 6.27, N 10.89

Found : C 48.32, H 6.44, N 10.86

Example 70

IR (KBr) : 3400, 1668.1, 1629.6, 1511.9  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7$ Hz), 1.06 (3H, d,  $J=5.7$ Hz), 1.15-1.5 (6H, m), 1.6-2.0 (7H, m), 2.1-2.65 (5H, m), 3.1-3.5 (9H, m), 3.6-4.5 (13H, m), 4.7-5.3 (11H, m), 5.46 (1H, d,  $J=5.9$ Hz), 6.73 (1H, d,  $J=8.2$ Hz), 6.81 (1H, s), 6.84 (1H, d,  $J=8.2$ Hz), 6.91 (2H, d,  $J=8.7$ Hz), 6.95-7.05 (3H, m), 7.09 (2H, d,  $J=8.7$ Hz), 7.25-7.5 (3H, m), 7.81 (2H, d,  $J=8.8$ Hz), 8.09 (1H, d,  $J=7$ Hz), 8.25 (1H, d,  $J=7$ Hz), 8.04 (1H, d,  $J=7$ Hz), 8.84 (1H, s)

FAB-MASS :  $m/z = 1327$  (M+Na)

Elemental Analysis Calcd. for  $C_{58}H_{77}N_{10}O_{21}SNa \cdot 5H_2O$  :

C 49.92, H 6.28, N 10.03

Found : C 49.75, H 6.41, N 10.25

224

Example 71

IR (KBr) : 3350, 1668.1, 1629.6, 1511.9, 1232.3  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.5\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.06 (3H, d,  $J=6.0\text{Hz}$ ), 1.2-1.4 (6H, m),  
5 1.4-1.6 (2H, m), 1.7-2.1 (3H, m), 2.1-2.7 (6H, m),  
3.1-3.5 (9H, m), 3.72 (2H, m), 3.8-4.5 (11H, m),  
4.7-5.3 (11H, m), 5.47 (1H, d,  $J=5.9\text{Hz}$ ), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.8-6.9 (2H, m), 6.91 (2H, d,  $J=8.6\text{Hz}$ ), 6.95-7.15 (5H, m), 7.25-7.5 (3H, m), 7.81  
10 (2H, d,  $J=8.8\text{Hz}$ ), 8.09 (1H, d,  $J=8.4\text{Hz}$ ), 8.26 (1H, d,  $J=7\text{Hz}$ ), 8.40 (1H, d,  $J=7\text{Hz}$ ), 8.84 (1H, s)

FAB-MASS :  $m/z$  = 1329 (M+Na)

Elemental Analysis Calcd. for  $\text{C}_{58}\text{H}_{79}\text{N}_{10}\text{NaO}_{21}\text{S}\cdot 6\text{H}_2\text{O}$  :

C 49.22, H 6.48, N 9.90

Found : C 49.33, H 6.67, N 9.89

Example 72

IR (KBr) : 3450, 1668.1, 1631.5, 1240.0  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.6\text{Hz}$ ), 1.05 (3H, d,  $J=5.6\text{Hz}$ ), 1.3-1.7 (4H, m), 1.7-2.1 (7H, m), 2.1-  
20 2.73 (6H, m), 2.75-3.05 (4H, m), 3.05-4.5 (18H, m),  
4.7-5.5 (12H, m), 6.72 (1H, d,  $J=8.3\text{Hz}$ ), 6.77-6.9 (2H, m), 6.96 (2H, d,  $J=8.6\text{Hz}$ ), 7.05 (1H, s), 7.1-  
7.5 (8H, m), 7.80 (2H, d,  $J=8.6\text{Hz}$ ), 8.06 (1H, d,  $J=8.4\text{Hz}$ ), 8.28 (1H, d,  $J=7\text{Hz}$ ), 8.41 (1H, d,  $J=7\text{Hz}$ ),  
25 8.84 (1H, s)

FAB-MASS :  $m/z$  = 1305 (M+Na)

Elemental Analysis Calcd. for  $\text{C}_{58}\text{H}_{78}\text{N}_{10}\text{O}_{21}\text{S}\cdot 8\text{H}_2\text{O}$  :

C 48.80, H 6.64, N 9.81

Found : C 48.88, H 6.50, N 9.81

Example 73

IR (KBr) : 1673.9, 1646.9, 1510.0 1238.1  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.4\text{Hz}$ ), 0.96 (3H, d,  $J=6.6\text{Hz}$ ), 1.05 (3H, d,  $J=5.6\text{Hz}$ ), 1.2-1.5 (6H, m),  
35

225

1.5-2.0 (9H, m), 2.1-2.8 (11H, m), 3.1-3.4 (5H, m),  
3.4-4.5 (17H, m), 4.6-5.5 (12H, m), 6.6-7.0 (9H,  
m), 7.04 (1H, s), 7.2-7.5 (3H, m), 7.78 (2H, d,  
J=8.7Hz), 8.05 (1H, d, J=8.4Hz), 8.24 (1H, d,  
J=7Hz), 8.39 (1H, d, J=7Hz), 8.84 (1H, s)

FAB-MASS :  $m/z = 1326 (M^+ - SO_3 + Na)$

Elemental Analysis Calcd. for  $C_{63}H_{89}N_{11}O_{22}S \cdot 9H_2O$  :

C 48.92, H 6.97, N 9.96

Found : C 48.77, H 6.73, N 9.94

#### Example 74

IR (KBr) : 3450, 1670.1, 1631.5, 1280.5  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.87 (3H, t, J=7.0Hz), 0.96 (3H, t,  
J=6.8Hz), 1.05 (3H, d, J=5.6Hz), 1.1-1.65 (13H, m),  
1.65-2.1 (7H, m), 2.1-2.65 (5H, m), 3.17 (1H, m),  
3.6-4.5 (13H, m), 4.7-5.3 (11H, m), 5.49 (1H, d,  
J=5.9Hz), 6.72 (1H, d, J=8.2Hz), 6.82 (1H, d,  
J=8.2Hz), 6.84 (1H, s), 7.04 (1H, s), 7.29 (2H, d,  
J=8.3Hz), 7.2-7.5 (3H, m), 7.80 (2H, d, J=8.3Hz),  
8.10 (1H, d, J=8.4Hz), 8.26 (1H, d, J=7Hz), 8.65  
(1H, d, J=7Hz), 8.84 (1H, s)

FAB-MASS :  $m/z = 1237 (M + Na)$

Elemental Analysis Calcd. for  $C_{53}H_{75}N_8O_{21}SNa \cdot 6H_2O$  :

C 48.10, H 6.63, N 8.47

Found : C 48.26, H 6.62, N 8.46

#### Example 75

IR (KBr) : 3400, 1670.1, 1627.6, 1272.8  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=3.3Hz), 1.08 (3H, d,  
J=5.7Hz), 1.2-1.6 (10H, m), 1.6-2.1 (5H, m), 2.1-  
2.7 (4H, m), 3.0-3.3 (1H, m), 3.20 (3H, s), 3.29  
(2H, t, J=6.4Hz), 3.73 (2H, m), 3.9-4.6 (13H, m),  
4.7-5.3 (11H, m), 5.53 (1H, d, J=5.8Hz), 6.73 (1H,  
d, J=8.3Hz), 6.83 (1H, d, J=8.3Hz), 6.91 (1H, s),  
7.05 (1H, s), 7.23 (1H, dd, J=9.0 and 2.3Hz), 7.3-

226

7.5 (4H, m), 7.8-8.0 (3H, m), 8.09 (1H, d, J=8.4Hz), 8.33 (1H, d, J=7Hz), 8.44 (1H, s), 8.80 (1H, d, J=7Hz), 8.85 (1H, s)

FAB-MASS :  $m/z = 1293$  (M+Na)

5 Elemental Analysis Calcd. for  $C_{55}H_{75}N_8O_{23}Na \cdot 6H_2O$  :  
C 47.89, H 6.36, N 8.12  
Found : C 47.81, H 6.26, N 8.05

Example 76

10 IR (KBr) : 3361.3, 1668.1, 1635.3, 1627.6  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t, J=6.7Hz), 0.96 (3H, d, J=6.7Hz), 1.09 (3H, d, J=5.8Hz), 1.19-1.25 (8H, m), 1.25-2.00 (5H, m), 2.02-2.53 (4H, m), 2.44 (3H, s), 2.61 (2H, t, J=7.6Hz), 3.05-3.27 (1H, m), 3.55-4.50 (13H, m), 4.65-5.65 (12H, m), 6.42 (1H, s), 6.65-6.95 (3H, m), 7.05 (1H, d, J=0.4Hz), 7.13-7.50 (5H, m), 7.50-7.88 (6H, m), 8.10 (1H, d, J=9.0Hz), 8.25 (1H, d, J=8.4Hz), 8.40 (1H, d, J=7.0Hz), 8.85 (1H, s)

20 FAB-MASS :  $m/z = 1299.3$  (M+Na-1)

Elemental Analysis Calcd. for  $C_{58}H_{77}N_8NaO_{21}S \cdot 5H_2O$  :  
C 50.94, H 6.41, N 8.19  
Found : C 50.99, H 6.40, N 8.15

25 Example 77

IR (Nujol) : 3351.7, 1670.1, 1652.7, 1623.8  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t, J=6.7Hz), 0.96 (3H, d, J=6.7Hz), 1.06 (3H, d, J=5.8Hz), 1.13-1.45 (8H, m), 1.47-1.96 (5H, m), 2.06-2.66 (8H, m), 2.81 (2H, t, J=7.6Hz), 3.04-3.30 (1H, m), 3.53-4.50 (13H, m), 4.53-5.70 (12H, m), 6.64-6.88 (3H, m), 7.04 (1H, d, J=0.4Hz), 7.13-7.60 (11H, m), 8.10 (1H, d, J=9.0Hz), 8.18 (1H, d, J=8.4Hz), 8.30 (1H, d, J=7.0Hz), 8.85 (1H, s)

35 FAB-MASS :  $m/z = 1287.4$  (M+Na-1)

227

Elemental Analysis Calcd. for  $C_{57}H_{77}N_8NaO_{21}S \cdot 5H_2O$  :

C 50.51, H 6.46, N 8.27

Found : C 50.84, H 6.60, N 8.33

5 Example 78

IR (KBr) : 3361.3, 1683.6, 1670.1, 1662.3, 1652.7,  
1646.9, 1635.3, 1627.6, 1623.8  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7Hz$ ), 1.07 (3H, d,  
10  $J=5.6Hz$ ), 1.28-2.00 (13H, m), 2.08-2.60 (4H, m),  
3.07-3.30 (1H, m), 3.60-4.66 (17H, m), 4.66-5.12  
(9H, m), 5.11 (1H, d,  $J=3.1Hz$ ), 5.25 (1H, d,  
 $J=4.6Hz$ ), 5.52 (1H, d,  $J=6.0Hz$ ), 6.62-6.95 (4H, m),  
6.95-7.15 (3H, m), 7.20-7.50 (3H, m), 7.50-7.85  
15 (7H, m), 8.12 (1H, d,  $J=8.4Hz$ ), 8.35 (1H, d,  
 $J=7.7Hz$ ), 8.53 (1H, d,  $J=7.0Hz$ ), 8.85 (1H, s)

FAB-MASS :  $m/z = 1319.7$  (M+Na-1)

Elemental Analysis Calcd. for  $C_{57}H_{74}N_8NaO_{22}SF \cdot 8H_2O$  :

C 47.49, H 6.29, N 7.77

Found : C 47.79, H 6.16, N 7.93

20 Example 79

IR (KBr) : 3354.9, 1668.1, 1662.3, 1654.6, 1646.9,  
1627.6  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.7Hz$ ), 0.90-1.10  
25 (6H, m), 1.10-1.40 (8H, m), 1.48-1.95 (5H, m),  
2.05-2.46 (4H, m), 2.60 (2H, t,  $J=7.6Hz$ ), 3.07-3.23  
(1H, m), 3.55-4.45 (14H, m), 4.67-5.32 (11H, m),  
5.48-5.63 (1H, m), 6.22 (1H, ,  $J=5.3Hz$ ), 6.65-6.89  
30 (3H, m), 6.97-7.15 (2H, m), 7.20-7.68 (10H, m),  
7.85-8.20 (3H, m), 8.84 (1H, s)

FAB-MASS :  $m/z = 1289.4$  (M+Na-1)

Elemental Analysis Calcd. for  $C_{56}H_{75}N_8NaO_{22}S \cdot 3H_2O$  :

C 50.90, H 6.18, N 8.48

Found : C 50.80, H 6.44, N 8.29

228

Example 80

IR (KBr) : 3361.3, 1664.3, 1631.5, 1600.6  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.7\text{Hz}$ ), 0.98 (3H, d,  $J=6.7\text{Hz}$ ), 1.16 (3H, t,  $J=5.9\text{Hz}$ ), 1.20-1.45 (8H, m), 1.50-1.70 (2H, m), 1.70-2.05 (3H, m), 2.10-2.57 (4H, m), 2.63 (2H, t,  $J=7.6\text{Hz}$ ), 3.10-3.30 (1H, m), 3.68-4.50 (13H, m), 4.78-5.32 (11H, m), 5.66 (1H, d,  $J=5.7\text{Hz}$ ), 6.68-7.02 (3H, m), 7.04 (1H, d,  $J=0.4\text{Hz}$ ), 7.25-7.48 (4H, m), 7.60-8.08 (7H, m), 8.10 (1H, d,  $J=8.4\text{Hz}$ ), 8.28 (1H, d,  $J=7.7\text{Hz}$ ), 8.85 (1H, s), 9.30 (1H, d,  $J=7.1\text{Hz}$ )

FAB-MASS :  $m/z = 1287.5$  ( $M+\text{Na}-1$ )

Elemental Analysis Calcd. for  $\text{C}_{55}\text{H}_{73}\text{N}_8\text{NaO}_{22}\text{S}\cdot 3\text{H}_2\text{O}$  :

C 50.53, H 6.09, N 8.57

Found : C 50.66, H 6.01, N 8.22

Example 81

IR (KBr) : 3349.7, 1668.1, 1627.6  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.7\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.09 (3H, d,  $J=5.8\text{Hz}$ ), 1.18-1.48 (8H, m), 1.50-2.10 (5H, m), 2.10-2.45 (3H, m), 2.50-2.65 (1H, m), 2.77 (2H, t,  $J=7.6\text{Hz}$ ), 3.05-3.25 (1H, m), 3.60-4.65 (13H, m), 4.67-5.60 (12H, m), 6.65-6.97 (3H, m), 7.05 (1H, d,  $J=0.4\text{Hz}$ ), 7.21-7.43 (4H, m), 7.76 (1H, s), 7.83-8.05 (3H, m), 8.10 (1H, d,  $J=9.0\text{Hz}$ ), 8.29 (1H, d,  $J=8.4\text{Hz}$ ), 8.48 (1H, s), 8.64-9.03 (2H, m)

FAB-MASS :  $m/z = 1233.0$  ( $M+\text{Na}-1$ )

Elemental Analysis Calcd. for  $\text{C}_{53}\text{H}_{71}\text{N}_8\text{NaO}_{20}\text{S}\cdot 3\text{H}_2\text{O}$  :

C 50.96, H 6.22, N 8.96

Found : C 50.62, H 6.40, N 8.92

Example 82

IR (KBr) : 3361.3, 1670.1, 1627.6  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.7\text{Hz}$ ), 0.96 (3H, d,

229



J=6.7Hz), 1.09 (3H, d, J=5.9Hz), 1.18-1.43 (6H, m),  
1.50-2.10 (5H, m), 2.10-2.69 (4H, m), 2.77 (2H, t,  
J=7.6Hz), 3.07-3.29 (1H, m), 3.60-4.62 (13H, m),  
4.69-5.23 (10H, m), 5.27 (1H, d, J=4.5Hz), 5.55  
(1H, d, J=5.9Hz), 6.68-7.00 (3H, m), 7.05 (1H, d,  
J=0.4Hz), 7.25-7.53 (4H, m), 7.76 (1H, s), 7.84-  
8.05 (3H, m), 8.13 (1H, d, J=8.4Hz), 8.33 (1H, d,  
J=7.7Hz), 8.48 (1H, s), 8.73-9.00 (2H, m)

FAB-MASS :  $m/z = 1219.4$  (M+Na-1)

Elemental Analysis Calcd. for  $C_{52}H_{69}N_8NaO_{21}S \cdot 5H_2O$  :

C 48.51, H 6.19, N 8.71

Found : C 48.67, H 6.34, N 8.74

Example 83

IR (KBr) : 3357.5, 1668.1, 1627.6  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d, J=6.7Hz), 1.07 (3H, d,  
J=6.0Hz), 1.20-1.62 (10H, m), 1.62-2.00 (5H, m),  
2.10-2.65 (4H, m), 3.20 (3H, s), 3.08-3.45 (1H, m),  
3.28 (2H, t, J=6.5Hz), 3.53-4.50 (15H, m), 4.68-  
5.13 (9H, m), 5.17 (1H, d, J=3.1Hz), 5.25 (1H, d,  
J=4.4Hz), 5.53 (1H, d, J=6.0Hz), 6.68-6.95 (4H, m),  
6.95-7.11 (3H, m), 7.20-7.52 (3H, m), 7.55-7.95  
(7H, m), 8.13 (1H, d, J=8.4Hz), 8.30 (1H, d,  
J=7.7Hz), 8.52 (1H, d, J=7.0Hz), 8.85 (1H, s)

FAB-MASS :  $m/z = 1345.2$  (M+Na-1)

Elemental Analysis Calcd. for  $C_{59}H_{79}N_8NaO_{23}S \cdot 8H_2O$  :

C 48.29, H 6.53, N 7.64

Found : C 48.44, H 6.58, N 7.75

Example 84

IR (KBr) : 3353.6, 1662.3, 1627.6  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.07 (3H, d,  
J=5.5Hz), 1.40-1.65 (2H, m), 1.65-2.00 (5H, m),  
2.00-2.67 (6H, m), 3.08-3.30 (1H, m), 3.50-4.50  
(15H, m), 4.68-5.13 (11H, m), 5.18 (1H, d,

230

J=3.1Hz), 5.26 (1H, d, J=4.5Hz), 5.53 (1H, d, J=6.0Hz), 5.70-6.00 (1H, m), 6.63-6.95 (4H, m), 6.95-7.13 (3H, m), 7.20-7.52 (3H, m), 7.52-7.95 (7H, m), 8.12 (1H, d, J=8.4Hz), 8.31 (1H, d, J=7.7Hz), 8.53 (1H, d, J=7.0Hz), 8.85 (1H, s)

FAB-MASS :  $m/z = 1285.4$  (M+Na-1)

Elemental Analysis Calcd. for  $C_{56}H_{71}N_8O_{22}SNa \cdot 8H_2O$  :

C 47.79, H 6.23, N 7.96

Found : C 47.59, H 6.32, N 8.06

#### Example 85

IR (KBr) : 3363.2, 1670.1, 1627.6  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (6H, d, J=6.5Hz), 0.96 (3H, d, J=6.7Hz), 1.07 (3H, d, J=5.7Hz), 1.22-1.41 (2H, m), 1.50-1.97 (6H, m), 2.11-2.65 (4H, m), 3.10-3.30 (1H, m), 3.60-4.50 (15H, m), 4.70-5.08 (8H, m), 5.10 (1H, d, J=5.6Hz), 5.16 (1H, d, J=3.1Hz), 5.25 (1H, d, J=4.5Hz), 5.50 (1H, d, J=5.9Hz), 6.65-6.92 (4H, m), 6.92-7.12 (3H, m), 7.21-7.50 (3H, m), 7.52-7.90 (7H, m), 8.12 (1H, d, J=8.4Hz), 8.30 (1H, d, J=7.7Hz), 8.56 (1H, d, J=7.0Hz), 8.85 (1H, s)

FAB-MASS :  $m/z = 1287.6$  (M+Na-1)

Elemental Analysis Calcd. for  $C_{56}H_{73}N_8NaO_{22}S \cdot 6.5H_2O$  :

C 48.66, H 6.27, N 8.11

Found : C 48.67, H 6.32, N 8.20

#### Example 86

IR (KBr) : 3361.3, 1683.6, 1670.1, 1654.6, 1635.3, 1623.8  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d, J=6.7Hz), 1.07 (3H, d, J=5.6Hz), 1.30-2.00 (11H, m), 2.10-2.70 (4H, m), 3.05-3.15 (1H, m), 3.55-4.70 (17H, m), 4.70-5.11 (9H, m), 5.16 (1H, d, J=3.1Hz), 5.25 (1H, d, J=4.5Hz), 5.52 (1H, d, J=6.0Hz), 6.65-6.95 (4H, m), 6.95-7.10 (3H, m), 7.10-7.50 (3H, m), 7.50-7.85

231

(7H, m), 8.12 (1H, d, J=8.4Hz), 8.30 (1H, d, J=8.3Hz), 8.52 (1H, d, J=7.0Hz), 8.85 (1H, s)

FAB-MASS :  $m/z = 1305.2$  (M+Na-1)

Elemental Analysis Calcd. for  $C_{56}H_{72}N_8NaO_{22}SF \cdot 6H_2O$  :

C 48.34, H 6.09, N 8.05

Found : C 48.47, H 6.29, N 7.95

Example 87

IR (KBr) : 3359.4, 1668.1, 1654.6, 1625.7  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d, J=6.7Hz), 1.07 (3H, d, J=6.0Hz), 1.22-1.62 (6H, m), 1.62-2.00 (5H, m), 2.10-2.65 (4H, m), 3.20 (3H, s), 3.05-3.40 (1H, m), 3.31 (2H, t, J=6.5Hz), 3.60-4.55 (15H, m), 4.65-5.13 (9H, m), 5.16 (1H, d, J=3.1Hz), 5.26 (1H, d, J=4.4Hz), 5.53 (1H, d, J=6.0Hz), 6.68-6.95 (4H, m), 6.95-7.20 (3H, m), 7.20-7.58 (3H, m), 7.58-7.90 (7H, m), 8.13 (1H, d, J=8.4Hz), 8.32 (1H, d, J=7.7Hz), 8.53 (1H, d, J=7.0Hz), 8.85 (1H, s)

FAB-MASS :  $m/z = 1317.6$  (M+Na-1)

Elemental Analysis Calcd. for  $C_{57}H_{75}N_8NaO_{23}S \cdot 7H_2O$  :

C 48.16, H 6.31, N 7.88

Found : C 48.21, H 6.60, N 7.78

Example 88

IR (KBr) : 3350, 2954, 1668, 1629, 1538, 1511, 1454, 1249  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.88 (3H, t, J=7.1Hz), 0.96 (3H, d, J=7.5Hz), 1.08 (2H, d, J=5.7Hz), 1.2-1.5 (6H, m), 1.6-2.4 (8H, m), 2.6-2.7 (1H, m), 3.1-3.3 (1H, m), 3.6-4.5 (19H, m), 4.7-5.3 (8H, m), 6.73 (1H, d, J=8.2Hz), 6.8-7.1 (5H, m), 7.19 (1H, s), 7.3-7.5 (3H, m), 7.75 (2H, d, J=8.7Hz), 7.8-8.0 (4H, m), 8.08 (1H, d, J=8.9Hz), 8.30 (1H, d, J=7.7Hz), 8.7-9.0 (3H, m)

FAB-MASS :  $m/z = 1327$  (M+Na<sup>+</sup>)

232

Elemental Analysis Calcd. for  $C_{57}H_{73}N_{10}O_{22}NaS \cdot 9H_2O$  :

C 46.65, H 6.25, N 9.54

Found : C 46.95, H 6.22, N 9.55

5 Example 89

IR (KBr) : 3376, 2931, 2858, 1662, 1631, 1521, 1444,  
1245, 1047  $cm^{-1}$

10 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7Hz$ ), 1.09 (3H, d,  
 $J=5.9Hz$ ), 1.3-1.6 (6H, m), 1.7-2.1 (5H, m), 2.2-2.4  
(3H, m), 2.5-2.6 (1H, m), 3.21 (3H, s), 3.2-3.4  
(3H, m), 3.6-4.5 (16H, m), 4.79 (2H, d,  $J=6.0Hz$ ),  
15 4.9-5.2 (5H, m), 5.10 (1H, d,  $J=3.6Hz$ ), 5.18 (1H,  
d,  $J=3.1Hz$ ), 5.26 (1H, d,  $J=4.5Hz$ ), 5.53 (1H, d,  
 $J=6.0Hz$ ), 6.73 (1H, d,  $J=8.2Hz$ ), 6.8-7.0 (2H, m),  
7.0-7.2 (3H, m), 7.3-7.5 (3H, m), 7.6-7.9 (8H, m),  
8.01 (2H, d,  $J=8.4Hz$ ), 8.12 (1H, d,  $J=8.4Hz$ ), 8.31  
(1H, d,  $J=7.7Hz$ ), 8.79 (1H, d,  $J=7.0Hz$ ), 8.85 (1H,  
s)

20 FAB-MASS :  $m/z = 1367 (M+Na^+)$

Elemental Analysis Calcd. for  $C_{61}H_{77}N_8O_{23}NaS \cdot 6.5H_2O$  :

C 50.10, H 6.20, N 7.66

Found : C 50.09, H 6.17, N 7.62

Example 90

25 IR (KBr) : 3363, 2937, 2869, 1646, 1444, 1255  $cm^{-1}$

30 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7Hz$ ), 1.08 (3H, d,  
 $J=5.7Hz$ ), 1.2-1.6 (10H, m), 1.7-2.1 (5H, m), 2.1-  
2.4 (3H, m), 2.5-2.7 (1H, m), 3.20 (3H, s), 3.2-3.4  
(1H, m), 3.6-4.6 (16H, m), 4.7-5.2 (8H, m), 5.16  
(1H, d,  $J=3.1Hz$ ), 5.24 (1H, d,  $J=4.5Hz$ ), 5.54 (1H,  
d,  $J=5.8Hz$ ), 6.73 (1H, d,  $J=8.2Hz$ ), 6.8-7.0 (2H,  
m), 7.1-7.4 (6H, m), 7.97 (2H, d,  $J=8.8Hz$ ), 8.0-8.4  
(6H, m), 8.84 (1H, s), 8.92 (1H, d,  $J=7.0Hz$ )

35 FAB-MASS :  $m/z = 1403.6 (M+Na^+)$

Elemental Analysis Calcd. for  $C_{59}H_{77}N_{10}O_{23}NaS_2 \cdot 6H_2O$  :

233

C 47.58, H 6.02, N 9.40

Found : C 47.72, H 6.12, N 9.42

Example 91

5 IR (KBr) : 3350, 1668, 1654, 1625, 1537, 1521, 1245,  
1047  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.9-1.1 (6H, m), 1.07 (3H, d,  
J=5.7Hz), 1.4-2.0 (7H, m), 2.2-2.5 (3H, m), 2.5-2.6  
(1H, m), 3.1-3.3 (1H, m), 3.6-4.5 (16H, m), 4.7-5.1  
10 (7H, m), 5.09 (1H, d, J=5.6Hz), 5.16 (1H, d,  
J=3.1Hz), 5.25 (1H, d, J=4.4Hz), 5.53 (1H, d,  
J=6.0Hz), 6.73 (1H, d, J=8.4Hz), 6.8-7.2 (6H, m)  
7.2-7.5 (4H, m), 7.5-7.8 (6H, m), 8.11 (1H, d,  
J=8.4Hz), 8.32 (1H, d, J=7.7Hz), 8.54 (1H, d,  
15 J=7.0Hz), 8.84 (1H, s)

FAB-MASS :  $m/z = 1259$  ( $M+Na^+$ )

Elemental Analysis Calcd. for  $C_{54}H_{69}N_8O_{22}Na \cdot 8H_2O$  :

C 46.95, H 6.20, N 8.11

Found : C 47.20, H 6.23, N 8.28

Example 92

IR (KBr) : 3359, 2929, 2852, 1668, 1650, 1631, 1538,  
1515  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.09 (3H, d,  
25 J=6.1Hz), 1.2-1.6 (5H, m), 1.6-2.5 (10H, m), 2.5-  
2.6 (1H, m), 3.18 (1H, m), 3.7-4.5 (15H, m), 4.8-  
5.2 (8H, m), 5.17 (1H, d, J=3.1Hz), 5.26 (1H, d,  
J=4.5Hz), 5.55 (1H, d, J=5.9Hz), 6.73 (1H, d,  
J=8.1Hz), 6.81 (1H, s), 6.85 (1H, s), 7.05 (1H, s),  
30 7.2-7.4 (3H, m), 7.45 (2H, d, J=8.2Hz), 7.96 (2H,  
d, J=8.2Hz), 8.0-8.2 (4H, s), 8.2-8.3 (1H, m), 8.85  
(1H, s), 8.9-9.0 (1H, d, J=7.0Hz)

FAB-MASS :  $m/z = 1327.5$  ( $M+Na$ ) $^+$

Elemental Analysis Calcd. for  $C_{56}H_{69}N_{10}O_{21}S_2Na \cdot 6H_2O$  :

C 47.59, H 5.78, N 9.91

234

Found : C 47.89, H 5.76, N 9.93

Example 93

IR (KBr) : 3350, 1654, 1629, 1517, 1249, 1047  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.9-1.1 (6H, m), 1.11 (3H, d,  $J=5.9\text{Hz}$ ), 1.6-2.0 (5H, s), 2.1-2.4 (3H, s), 2.6-2.7 (1H, m), 3.1-3.3 (1H, m), 3.6-4.5 (16H, m), 4.7-5.2 (7H, m), 5.10 (1H, d,  $J=5.6\text{Hz}$ ), 5.17 (1H, d,  $J=3.1\text{Hz}$ ), 5.25 (1H, d,  $J=4.5\text{Hz}$ ), 5.55 (1H, d,  $J=5.7\text{Hz}$ ), 6.7-6.9 (3H, m), 7.0-7.5 (6H, m), 7.74 (2H, d,  $J=8.8\text{Hz}$ ), 7.91 (2H, d,  $J=8.5\text{Hz}$ ), 8.1-8.4 (8H, m), 8.84 (1H, s), 8.97 (1H, d,  $J=7.0\text{Hz}$ )

FAB-MASS :  $m/z = 1363.5$  ( $\text{M}+\text{Na}$ ) $^+$

Elemental Analysis Calcd. for  $\text{C}_{59}\text{H}_{69}\text{N}_{10}\text{O}_{23}\text{SNa}\cdot 5\text{H}_2\text{O}$  :

C 49.51, H 5.56, N 9.79

Found : C 49.39, H 5.63, N 9.77

Example 94

IR (KBr) : 3355, 2929, 2856, 1664, 1631, 1519, 1440, 1282  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.84 (3H, t,  $J=6.7\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.07 (3H, t,  $J=5.8\text{Hz}$ ), 1.2-1.5 (12H, m), 1.7-2.0 (5H, m), 2.2-2.4 (3H, m), 2.5-2.7 (1H, m), 2.94 (2H, t,  $J=7.4\text{Hz}$ ), 3.1-3.3 (1H, m), 3.6-4.6 (14H, m), 4.8-5.2 (7H, m), 5.10 (1H, d,  $J=3.6\text{Hz}$ ), 5.17 (1H, d,  $J=3.1\text{Hz}$ ), 5.26 (1H, d,  $J=4.5\text{Hz}$ ), 5.55 (1H, d,  $J=5.9\text{Hz}$ ), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.8-7.0 (2H, m), 7.0-7.5 (4H, m), 8.0-8.2 (5H, m), 8.27 (1H, d,  $J=7.7\text{Hz}$ ), 8.85 (1H, s), 8.93 (1H, d,  $J=7.0\text{Hz}$ )

FAB-MASS :  $m/z = 1279$  ( $\text{M}+\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{53}\text{H}_{73}\text{N}_{10}\text{O}_{22}\text{SNa}\cdot 5.5\text{H}_2\text{O}$  :

C 46.93, H 6.24, N 10.33

Found : C 46.93, H 6.46, N 10.31

235

Example 95

IR (KBr) : 3363, 1673, 1648, 1538, 1253  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.92 (3H, t,  $J=6.8\text{Hz}$ ), 0.97 (3H, d,  $J=6.8\text{Hz}$ ), 1.10 (3H, d,  $J=5.8\text{Hz}$ ), 1.2-1.5 (6H, m), 1.7-2.1 (5H, m), 2.1-2.4 (3H, m), 2.5-2.6 (1H, m), 3.1-3.3 (1H, m), 3.6-4.5 (16H, m), 4.7-5.1 (9H, m), 5.16 (1H, d,  $J=3.1\text{Hz}$ ), 5.24 (1H, d,  $J=4.5\text{Hz}$ ), 5.54 (1H, d,  $J=5.8\text{Hz}$ ), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.8-7.4 (8H, m), 8.04 (2H, d,  $J=8.8\text{Hz}$ ), 8.13 (2H, d,  $J=8.6\text{Hz}$ ), 8.2-8.4 (4H, m), 8.84 (1H, s), 8.98 (1H, d,  $J=7.0\text{Hz}$ )

FAB-MASS :  $m/z = 1329.6$  ( $M+\text{Na}$ ) $^+$

Elemental Analysis Calcd. for  $\text{C}_{56}\text{H}_{71}\text{N}_{10}\text{O}_{23}\text{SNa}\cdot 7\text{H}_2\text{O}$  :

C 46.92, H 5.97, N 9.77

Found : C 46.86, H 5.99, N 9.77

Example 96

IR (KBr) : 3355, 2929, 1666, 1648, 1631, 1515, 1442, 1047  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.7\text{Hz}$ ), 0.97 (3H, d,  $J=6.7\text{Hz}$ ), 1.10 (3H, d,  $J=5.8\text{Hz}$ ), 1.2-1.5 (10H, m), 1.7-2.1 (5H, m), 2.1-2.4 (3H, m), 2.5-2.6 (1H, m), 3.1-3.3 (1H, m), 3.6-4.6 (16H, m), 4.79 (2H, d,  $J=5.9\text{Hz}$ ), 4.8-5.2 (5H, m), 5.09 (1H, d,  $J=5.5\text{Hz}$ ), 5.16 (1H, d,  $J=3.1\text{Hz}$ ), 5.23 (1H, d,  $J=4.5\text{Hz}$ ), 5.53 (1H, d,  $J=5.9\text{Hz}$ ), 6.73 (1H, d,  $J=8.0\text{Hz}$ ), 6.8-6.9 (2H, m), 7.0-7.5 (6H, m), 7.97 (2H, d,  $J=8.8\text{Hz}$ ), 8.0-8.3 (6H, m), 8.83 (1H, s), 8.88 (1H, d,  $J=7.0\text{Hz}$ )

FAB-MASS :  $m/z = 1373.5$  ( $M+\text{Na}$ ) $^+$

Elemental Analysis Calcd. for  $\text{C}_{58}\text{H}_{75}\text{N}_{10}\text{O}_{22}\text{S}_2\text{Na}\cdot 6\text{H}_2\text{O}$  :

C 47.73, H 6.01, N 9.60

Found : C 47.57, H 5.92, N 9.53

Example 97

236

IR (KBr) : 3361, 2925, 2852, 1668, 1650, 1631, 1538,  
1452, 1049  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.9\text{Hz}$ ), 0.96 (3H, d,  
 $J=6.7\text{Hz}$ ), 1.08 (3H, d,  $J=5.7\text{Hz}$ ), 1.2-1.4 (11H, m),  
1.4-1.6 (2H, m), 1.7-2.1 (5H, m), 2.1-2.5 (5H, m),  
2.5-2.6 (1H, m), 3.1-3.3 (2H, m), 3.7-4.5 (14H, m),  
4.7-5.0 (7H, m), 5.09 (1H, d,  $J=5.6\text{Hz}$ ), 5.16 (1H,  
d,  $J=3.1\text{Hz}$ ), 5.25 (1H, d,  $J=4.5\text{Hz}$ ), 5.54 (1H, d,  
 $J=5.8\text{Hz}$ ), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.8-7.0 (2H, d),  
7.04 (1H, s), 7.2-7.5 (3H, m), 8.03 (4H, s), 8.0-  
8.3 (2H, m), 8.84 (1H, s), 8.95 (1H, d,  $J=7.0\text{Hz}$ )

FAB-MASS :  $m/z = 1321.9$  ( $M+\text{Na}$ ) $^+$

Elemental Analysis Calcd. for  $\text{C}_{55}\text{H}_{75}\text{N}_{10}\text{O}_{21}\text{S}_2\text{Na}\cdot 5\text{H}_2\text{O}$  :  
C 47.54, H 6.17, N 10.08  
Found : C 47.38, H 6.12, N 9.98

Example 98

IR (KBr) : 3374, 2937, 2875, 1658, 1629, 1531, 1436,  
1255, 1047  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.9-1.11 (6H, m), 1.09 (3H, d,  
 $J=5.7\text{Hz}$ ), 1.2-1.5 (4H, m), 1.7-2.1 (5H, m), 2.2-2.5  
(3H, m), 2.6-2.7 (1H, m), 3.2-3.3 (1H, m), 3.6-4.5  
(16H, m), 4.80 (2H, d,  $J=5.8\text{Hz}$ ), 4.8-5.2 (5H, m),  
5.10 (1H, d,  $J=5.5\text{Hz}$ ), 5.17 (1H, d,  $J=3.0\text{Hz}$ ), 5.24  
(1H, d,  $J=4.5\text{Hz}$ ), 5.53 (1H, d,  $J=5.8\text{Hz}$ ), 6.73 (1H,  
d,  $J=8.2\text{Hz}$ ), 6.8-7.0 (2H, m), 7.06 (1H, s), 7.10  
(2H, d,  $J=8.9\text{Hz}$ ), 7.2-7.5 (3H, m), 7.68 (1H, s),  
7.86 (2H, d,  $J=8.8\text{Hz}$ ), 8.0-8.4 (6H, m), 8.84 (1H,  
s), 8.90 (1H, d,  $J=7.0\text{Hz}$ )

FAB-MASS :  $m/z = 1314$  ( $M+\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{56}\text{H}_{70}\text{N}_9\text{O}_{23}\text{NaS}\cdot 6\text{H}_2\text{O}$  :  
C 48.03, H 5.90, N 9.00  
Found : C 47.92, H 5.83, N 8.88

Example 99

237



IR (KBr) : 3345, 1646, 1633, 1531, 1257  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7\text{Hz}$ ), 1.11 (3H, d,  $J=5.7\text{Hz}$ ), 1.2-1.6 (10H, m), 1.7-2.5 (8H, m), 2.6-2.7 (1H, m), 3.21 (3H, s), 3.3-3.4 (1H, m), 3.7-4.6 (16H, m), 4.8-5.2 (8H, m), 5.16 (1H, d,  $J=3.1\text{Hz}$ ), 5.24 (1H, d,  $J=4.5\text{Hz}$ ), 5.55 (1H, d,  $J=5.7\text{Hz}$ ), 6.7-6.9 (3H, m), 7.0-7.5 (6H, m), 8.0-8.3 (8H, m), 8.84 (1H, s), 8.96 (1H, d,  $J=7.0\text{Hz}$ )

FAB-MASS :  $m/z = 1387.7$  ( $M+\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{59}\text{H}_{77}\text{N}_{10}\text{O}_{24}\text{NaS}\cdot 6\text{H}_2\text{O}$  :

C 48.09, H 6.09, N 9.51

Found : C 47.81, H 5.83, N 9.38

Example 100

IR (KBr) : 3357, 1668, 1631, 1429, 1284, 1047  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7\text{Hz}$ ), 1.09 (3H, d,  $J=5.8\text{Hz}$ ), 1.8-2.4 (6H, m), 2.5-2.6 (1H, m), 3.1-3.2 (1H, m), 3.7-4.6 (14H, m), 4.7-5.2 (7H, m), 5.10 (1H, d,  $J=5.5\text{Hz}$ ), 5.17 (1H, d,  $J=3.1\text{Hz}$ ), 5.24 (1H, d,  $J=5.5\text{Hz}$ ), 5.53 (1H, d,  $J=5.8\text{Hz}$ ), 6.75 (1H, d,  $J=8.2\text{Hz}$ ), 6.8-6.9 (2H, m), 7.05 (1H, s), 7.3-7.6 (9H, m), 7.8-7.9 (4H, m), 8.0-8.2 (5H, m), 8.2-8.3 (1H, m), 8.34 (1H, d,  $J=9.3\text{Hz}$ ), 8.7-8.8 (1H, m), 8.85 (1H, s)

FAB-MASS :  $m/z = 1332.7$  ( $M+\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{58}\text{H}_{65}\text{N}_{10}\text{O}_{22}\text{SNa}\cdot 8\text{H}_2\text{O}$  :

C 47.93, H 5.62, N 9.64

Found : C 47.83, H 5.53, N 9.56

Example 101

IR (KBr) : 3353, 2929, 2856, 1666, 1631, 1612, 1496, 1440, 1259  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.6\text{Hz}$ ), 0.97 (3H, d,  $J=6.5\text{Hz}$ ), 1.09 (3H, d,  $J=5.9\text{Hz}$ ), 1.2-1.5 (10H, m), 1.7-2.1 (5H, m), 2.2-2.5 (3H, m), 2.6-2.7 (1H, m),

238

3.1-3.2 (1H, m), 3.6-4.5 (16H, m), 4.7-5.0 (3H, m),  
5.0-5.2 (5H, m), 5.10 (1H, d, J=3.1Hz), 5.26 (1H,  
d, J=4.2Hz), 5.56 (1H, d, J=5.5Hz), 6.73 (1H, d,  
J=8.1Hz), 6.8-7.0 (2H, m), 7.05 (1H, s), 7.1-7.5  
(5H, m), 8.0-8.4 (8H, m), 8.85 (1H, s), 8.95 (1H, d,  
J=7.0Hz)

FAB-MASS :  $m/z = 1357.3$  ( $M+Na^+$ )

Elemental Analysis Calcd. for  $C_{58}H_{75}N_{10}O_{23}NaS \cdot 7H_2O$  :

C 47.67, H 6.14, N 9.58

Found : C 47.63, H 6.42, N 9.52

Example 102

IR (KBr) : 3361, 1670, 1648, 1633, 1540, 1519,  
1249  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (3H, t, J=7.0Hz), 0.97 (3H, d,  
J=6.8Hz), 1.10 (3H, d, J=5.7Hz), 1.2-1.5 (6H, m),  
1.6-2.4 (8H, m), 2.5-2.7 (1H, m), 3.1-3.3 (1H, m),  
3.6-4.5 (16H, m), 4.80 (2H, d, J=5.8Hz), 4.8-5.2  
(5H, m), 5.10 (1H, d, J=5.4Hz), 5.18 (1H, d,  
J=3.1Hz), 5.25 (1H, d, J=4.3Hz), 5.55 (1H, d,  
J=5.7Hz), 6.73 (1H, d, J=8.2Hz), 6.8-7.0 (2H, m),  
7.0-7.5 (6H, m), 8.02 (1H, d, J=5.3Hz), 8.0-8.4  
(4H, m), 8.42 (2H, d, J=8.4Hz), 8.48 (2H, d,  
J=8.9Hz), 8.8-9.0 (3H, m)

FAB-MASS :  $m/z = 1339.3$  ( $M+Na^+$ )

Elemental Analysis Calcd. for  $C_{58}H_{73}N_{10}O_{22}SNa \cdot 6H_2O$  :

C 48.87, H 6.01, N 9.83

Found : C 49.16, H 5.92, N 9.86

Example 103

IR (KBr) : 3350, 2971, 2859, 1672, 1629, 1537, 1442,  
1247, 1047  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.8Hz), 1.0-1.2 (6H,  
m), 1.2-1.6 (12H, m), 1.7-2.5 (8H, m), 2.5-2.6 (1H,  
m), 3.2-3.6 (7H, m), 3.7-4.5 (16H, m), 4.76 (2H, d,

239

J=5.6Hz), 4.8-5.1 (5H, m), 5.09 (1H, d, J=5.5Hz),  
5.16 (1H, d, J=3.1Hz), 5.23 (1H, d, J=5.5Hz), 5.51  
(1H, d, J=5.9Hz), 6.73 (1H, d, J=8.2Hz), 6.8-6.9  
(2H, m), 7.0-7.1 (3H, m), 7.3-7.5 (3H, m), 7.67  
(2H, d, J=6.9Hz), 7.71 (2H, d, J=6.9Hz), 7.95 (2H,  
d, J=8.4Hz), 8.05 (1H, d, J=7.0Hz), 8.23 (1H, d,  
J=7.7Hz), 8.70 (1H, d, J=7.0Hz), 8.84 (1H, s)

FAB-MASS :  $m/z = 1377.1$  ( $M+Na^+$ )

Elemental Analysis Calcd. for  $C_{60}H_{83}N_8O_{24}NaS \cdot 5H_2O$  :

C 49.86, H 6.49, N 7.75

Found : C 49.74, H 6.73, N 7.68

Example 104

IR (KBr) : 3349, 2937, 2858, 1672, 1629, 1537, 1444,  
1249, 1047  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.08 (3H, d,  
J=5.6Hz), 1.2-1.7 (14H, m), 1.7-2.1 (5H, m), 2.1-  
2.4 (5H, m), 2.5-2.6 (1H, m), 3.1-3.2 (1H, m), 3.4-  
3.6 (4H, m), 3.7-4.5 (16H, m), 4.77 (2H, d,  
J=5.7Hz), 4.8-5.2 (5H, m), 5.09 (1H, d, J=5.6Hz),  
5.16 (1H, d, J=3.1Hz), 5.24 (1H, d, J=4.5Hz), 5.51  
(1H, d, J=5.8Hz), 6.73 (1H, d, J=8.2Hz), 6.8-6.9  
(2H, m), 7.0-7.1 (3H, m), 7.3-7.5 (3H, m), 7.6-7.8  
(4H, m), 7.96 (2H, d, J=8.4Hz), 8.10 (1H, d,  
J=8.4Hz), 8.24 (1H, d, J=7.7Hz), 8.71 (1H, d,  
J=7.0Hz), 8.89 (1H, s)

FAB-MASS :  $m/z = 1386.5$  ( $M+Na^+$ )

Elemental Analysis Calcd. for  $C_{61}H_{82}N_9O_{23}NaS \cdot 6H_2O$  :

C 49.76, H 6.43, N 8.56

Found : C 49.99, H 6.39, N 8.52

Example 105

IR (KBr) : 3350, 2933, 2856, 1664, 1631, 1604, 1511,  
1450, 1243, 1045  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t, J=6.7Hz), 0.96 (3H, d,

240

J=6.5Hz), 1.05 (3H, d, J=5.7Hz), 1.2-1.5 (8H, m),  
1.6-2.0 (5H, m), 2.1-2.4 (3H, m), 2.5-2.6 (1H, m),  
3.0-3.3 (5H, m), 3.6-4.4 (20H, m), 4.7-5.1 (7H, m),  
5.10 (1H, d, J=5.5Hz), 5.16 (1H, d, J=3.1Hz), 5.27  
(1H, d, J=4.5Hz), 5.51 (1H, d, J=6.0Hz), 6.7-7.1  
(9H, m), 7.2-7.5 (3H, m), 8.0-8.2 (2H, m), 8.2-8.4  
(1H, m), 8.4-8.6 (1H, m), 8.66 (1H, d, J=2.2Hz),  
8.85 (1H, s)

FAB-MASS :  $m/z = 1360$  ( $M+Na^+$ )

Elemental Analysis Calcd. for  $C_{58}H_{80}N_{11}O_{22}SNa \cdot 6H_2O$  :

C 48.16, H 6.41, N 10.65

Found : C 47.91, H 6.31, N 10.56

Example 106

IR (KBr) : 3369, 3345, 2935, 1672, 1629, 1511, 1245,  
1047  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.06 (3H, d,  
J=5.8Hz), 1.3-1.6 (10H, m), 1.6-2.0 (5H, m), 2.1-  
2.4 (3H, m), 2.5-2.6 (1H, m), 3.20 (3H, s), 3.28  
(2H, t, J=6.4Hz), 3.1-3.4 (5H, m), 3.7-4.5 (20H,  
m), 4.7-5.1 (7H, m), 5.08 (1H, d, J=5.5Hz), 5.15  
(1H, d, J=3.1Hz), 5.23 (1H, d, J=4.5Hz), 5.48 (1H,  
d, J=5.8Hz), 6.73 (1H, d, J=8.2Hz), 6.82 (2H, d,  
J=9.1Hz), 6.94 (2H, d, J=9.1Hz), 6.9-7.0 (1H, m),  
7.04 (1H, s), 7.3-7.5 (3H, m), 8.0-8.1 (2H, m),  
8.27 (1H, d, J=7.7Hz), 8.49 (1H, d, J=7.0Hz), 8.66  
(1H, d, J=2.2Hz), 8.84 (1H, s)

FAB-MASS :  $m/z = 1404$  ( $M+Na^+$ )

Example 107

IR (KBr) : 3357, 1647, 1631, 1537, 1444, 1249,  
1049  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.9-1.1 (6H, m), 1.09 (3H, d,  
J=5.9Hz), 1.6-2.4 (8H, m), 2.4-2.5 (1H, m), 3.1-3.3  
(1H, m), 3.6-4.5 (16H, m), 4.8-5.2 (7H, m), 5.10

241

(1H, d, J=5.6Hz), 5.17 (1H, d, J=3.1Hz), 5.25 (1H, d, J=4.5Hz), 5.55 (1H, d, J=5.9Hz), 6.73 (1H, d, J=8.2Hz), 6.8-7.0 (2H, m), 7.0-7.6 (6H, m), 7.73 (2H, d, J=8.7Hz), 7.86 (2H, d, J=8.5Hz), 8.0-8.3 (8H, m), 8.84 (1H, s), 8.9-9.0 (1H, m)

FAB-MASS :  $m/z = 1379.4$  (M+Na)<sup>+</sup>

Elemental Analysis Calcd. for C<sub>59</sub>H<sub>69</sub>N<sub>10</sub>O<sub>22</sub>S<sub>2</sub>Na·6H<sub>2</sub>O :

C 48.36, H 5.57, N 9.56

Found : C 48.18, H 5.60, N 9.36

The Object Compounds (108) to (117) were obtained according to a similar manner to that of Example 27.

Example 108

IR (KBr) : 3350, 2933, 1670, 1627, 1521, 1436, 1272, 1047 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.85 (3H, t, J=6.7Hz), 0.92 (3H, d, J=6.7Hz), 1.1-1.4 (11H, m), 1.7-2.4 (9H, m), 3.1-3.2 (1H, m), 3.5-5.4 (27H, m), 6.6-7.2 (8H, m), 7.5-7.8 (3H, m), 7.8-8.0 (3H, m), 8.1-8.8 (3H, m)

FAB-MASS :  $m/z = 1249.4$  (M+Na)<sup>+</sup>

Elemental Analysis Calcd. for C<sub>52</sub>H<sub>71</sub>N<sub>10</sub>O<sub>21</sub>NaS·7H<sub>2</sub>O :

C 46.15, H 6.33, N 10.35

Found : C 46.12, H 6.35, N 10.24

Example 109

IR (Kbr pelet) : 3361, 2933, 2856, 1670, 1652, 1616, 1540, 1508, 1448, 1261, 1047 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.86 (3H, t, J=6.6Hz), 0.97 (3H, d, J=6.8Hz), 1.12 (3H, d, J=6.8Hz), 1.2-1.5 (10H, m), 1.7-2.0 (5H, m), 2.2-2.6 (4H, m), 3.1-3.2 (1H, m), 3.7-4.4 (16H, m), 4.8-5.3 (10H, m), 5.59 (1H, d, J=6.0Hz), 6.7-6.9 (3H, m), 7.0-7.4 (7H, m), 7.8-8.2 (4H, m), 8.8-9.0 (2H, m)

FAB-MASS :  $m/z = 1280.3$  (M+Na)<sup>+</sup>

247

Elemental Analysis Calcd. for  $C_{54}H_{72}N_9O_{23}NaS \cdot 7H_2O$  :

C 46.45, H 6.21, N 9.03

Found : C 46.68, H 6.44, N 9.03

5 Example 110

IR (KBr) : 3350, 2931, 1670, 1627, 1540, 1436, 1276,  
1047  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.8Hz$ ), 0.93 (2H, d,  
 $J=8.8Hz$ ), 1.08 (2H, d,  $J=5.9Hz$ ), 1.2-1.4 (4H, m),  
10 1.5-1.7 (2H, m), 1.7-2.1 (3H, m), 2.1-2.4 (3H, m),  
2.6-2.7 (3H, m), 3.1-3.3 (1H, m), 3.6-4.5 (17H, m),  
4.7-5.4 (8H, m), 6.73 (1H, d,  $J=8.2Hz$ ), 6.83 (2H,  
d,  $J=8.2Hz$ ), 7.0-7.1 (1H, m), 7.2-7.5 (5H, m), 7.65  
15 (2H, d,  $J=8.2Hz$ ), 7.74 (2H, d,  $J=8.4Hz$ ), 7.98 (2H,  
d,  $J=8.4Hz$ ), 8.08 (1H, d,  $J=8.5Hz$ ), 8.25 (1H, d,  
 $J=8.5Hz$ ), 8.74 (1H, d,  $J=7.6Hz$ ), 8.7-9.0 (1H, br)

FAB-MASS :  $m/z = 1231.2$  ( $M+Na^+$ )

Elemental Analysis Calcd. for  $C_{53}H_{69}N_8O_{21}NaS \cdot 3H_2O$  :

C 50.39, H 5.98, N 8.87

20 Found : C 50.34, H 6.25, N 8.90

Example 111

IR (KBr) : 3353.6, 1670.1, 1652.7, 1623.8  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7Hz$ ), 1.07 (3H, d,  
25  $J=5.6Hz$ ), 1.20-1.62 (8H, m), 1.62-2.00 (5H, m),  
2.10-2.65 (4H, m), 3.20 (3H, s), 3.08-3.40 (1H, m),  
3.30 (2H, t,  $J=6.5Hz$ ), 3.53-4.50 (15H, m), 4.68-  
5.13 (9H, m), 5.16 (1H, d,  $J=2.9Hz$ ), 5.26 (1H, d,  
 $J=4.5Hz$ ), 5.53 (1H, d,  $J=5.9Hz$ ), 6.68-6.95 (4H, m),  
30 6.95-7.11 (3H, m), 7.20-7.52 (3H, m), 7.55-7.95  
(7H, m), 8.13 (1H, d,  $J=8.4Hz$ ), 8.31 (1H, d,  
 $J=7.7Hz$ ), 8.53 (1H, d,  $J=7.0Hz$ ), 8.85 (1H, s)

FAB-MASS :  $m/z = 1331.5$  ( $M+Na-1$ )

Elemental Analysis Calcd. for  $C_{58}H_{77}N_8NaO_{23}S \cdot 6H_2O$  :

35 C 49.15, H 6.33, N 7.91

243

Found : C 49.07, H 6.53, N 7.84

Example 112

IR (KBr) : 3350, 2937, 1673, 1646, 1631, 1538, 1519,  
1456, 1247, 1049  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.6\text{Hz}$ ), 1.07 (3H, d,  
 $J=5.7\text{Hz}$ ), 1.3-2.4 (25H, m), 2.5-2.6 (1H, m), 3.2-  
3.4 (1H, m), 3.5-4.6 (20H, m), 4.8-5.7 (11H, m),  
6.73 (1H, d,  $J=8.0\text{Hz}$ ), 6.9-7.0 (2H, m), 7.0-7.2  
(3H, m), 7.3-7.6 (3H, m), 7.74 (2H, d,  $J=8.5\text{Hz}$ ),  
7.77 (2H, d,  $J=8.3\text{Hz}$ ), 8.02 (2H, d,  $J=8.3\text{Hz}$ ), 8.13  
(1H, d,  $J=8.4\text{Hz}$ ), 8.30 (1H, d,  $J=7.7\text{Hz}$ ), 8.77 (1H,  
d,  $J=7.0\text{Hz}$ ), 8.85 (1H, s)

FAB-MASS :  $m/z = 1389$  ( $M+\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{61}\text{H}_{83}\text{N}_8\text{O}_{24}\text{NaS}\cdot 7\text{H}_2\text{O}$  :

C 49.06, H 6.55, N 7.50

Found : C 49.03, H 6.54, N 7.56

Example 113

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.84 (3H, t,  $J=6.7\text{Hz}$ ), 0.96 (3H, d,  
 $J=6.7\text{Hz}$ ), 1.07 (3H, d,  $J=5.9\text{Hz}$ ), 1.1-1.3 (14H, m),  
1.7-2.1 (5H, m), 2.2-2.5 (3H, m), 2.6-2.7 (1H, m),  
3.1-3.3 (1H, m), 3.7-4.5 (16H, m), 4.7-5.1 (7H, m),  
5.10 (1H, d,  $J=5.5\text{Hz}$ ), 5.16 (1H, d,  $J=3.1\text{Hz}$ ), 5.25  
(1H, d,  $J=4.5\text{Hz}$ ), 5.49 (1H, d,  $J=5.7\text{Hz}$ ), 6.53 (1H,  
d,  $J=3.1\text{Hz}$ ), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.8-6.9 (2H,  
m), 7.05 (1H, m), 7.31 (1H, d,  $J=8.1\text{Hz}$ ), 7.4-7.6  
(4H, m), 7.70 (1H, d,  $J=6.7\text{Hz}$ ), 8.08 (1H, d,  
 $J=8.4\text{Hz}$ ), 8.18 (1H, s), 8.31 (1H, d,  $J=7.7\text{Hz}$ ), 8.57  
(1H, d,  $J=7.0\text{Hz}$ ), 8.85 (1H, s)

FAB-MASS :  $m/z = 1264$  ( $M+\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{54}\text{H}_{76}\text{N}_9\text{O}_{21}\text{NaS}\cdot 6\text{H}_2\text{O}$  :

C 48.03, H 6.57, N 9.34

Found : C 48.02, H 6.61, N 9.28

244

Example 114

IR (KBr) : 3350, 2937, 1668, 1631, 1537, 1247, 1047  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=7.4\text{Hz}$ ), 0.96 (3H, d,  $J=6.5\text{Hz}$ ), 1.07 (3H, d,  $J=5.7\text{Hz}$ ), 1.3-1.7 (7H, m), 1.7-2.1 (5H, m), 2.2-2.4 (3H, m), 2.6-2.7 (1H, m), 3.0-3.8 (16H, m), 3.8-4.6 (11H, m), 4.7-5.3 (6H, m), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.8-7.0 (2H, m), 7.0-7.2 (3H, m), 7.3-7.5 (3H, m), 7.6-7.8 (4H, m), 7.96 (2H, d,  $J=8.3\text{Hz}$ ), 8.11 (1H, d,  $J=8.2\text{Hz}$ ), 8.26 (1H, d,  $J=7.6\text{Hz}$ ), 8.6-9.0 (2H, m)

FAB-MASS :  $m/z = 1319.4$  ( $M+\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{57}\text{H}_{77}\text{N}_8\text{O}_{23}\text{NaS}\cdot 8\text{H}_2\text{O}$  :

C 47.50, H 6.50, N 7.77

Found : C 47.72, H 6.85, N 7.85

Example 115

IR (KBr) : 3350, 1666, 1631, 1546, 1276, 1247  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=7.5\text{Hz}$ ), 1.08 (3H, d,  $J=5.7\text{Hz}$ ), 1.4-1.6 (4H, m), 1.6-2.1 (5H, m), 2.1-2.4 (3H, m), 2.5-2.6 (1H, m), 3.1-3.3 (1H, m), 3.23 (3H, s), 3.3-3.5 (2H, m), 3.7-4.5 (16H, m), 4.79 (2H, d,  $J=6.2\text{Hz}$ ), 4.8-5.1 (5H, m), 5.11 (1H, d,  $J=5.6\text{Hz}$ ), 5.18 (1H, d,  $J=3.1\text{Hz}$ ), 5.26 (1H, d,  $J=4.4\text{Hz}$ ), 5.54 (1H, d,  $J=5.7\text{Hz}$ ), 6.73 (1H, d,  $J=8.1\text{Hz}$ ), 6.8-7.0 (2H, m), 7.0-7.1 (3H, m), 7.3-7.5 (3H, m), 7.6-7.9 (8H, m), 8.01 (2H, d,  $J=8.4\text{Hz}$ ), 8.08 (1H, d,  $J=8.4\text{Hz}$ ), 8.32 (1H, d,  $J=7.7\text{Hz}$ ), 8.80 (1H, d,  $J=7.0\text{Hz}$ ), 8.85 (1H, s)

FAB-MASS :  $m/z = 1353.9$  ( $M+\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{60}\text{H}_{75}\text{N}_8\text{O}_{23}\text{NaS}\cdot 9.5\text{H}_2\text{O}$  :

C 47.96, H 6.31, N 7.46

Found : C 47.97, H 6.25, N 7.41

Example 116

IR (KBr) : 3450, 2935, 1675, 1650, 1540, 1513, 1454,

245



1047  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7\text{Hz}$ ), 1.09 (3H, d,  $J=5.9\text{Hz}$ ), 1.60 (6H, s), 1.7-2.4 (6H, m), 2.5-2.6 (1H, m), 3.1-3.6 (5H, m), 3.7-4.5 (14H, m), 4.7-5.0 (3H, m), 5.0-5.2 (4H, m), 5.11 (1H, d,  $J=5.5\text{Hz}$ ), 5.18 (1H, d,  $J=3.1\text{Hz}$ ), 5.26 (1H, d,  $J=4.5\text{Hz}$ ), 5.56 (1H, d,  $J=6.0\text{Hz}$ ), 6.8-7.5 (9H, m), 7.84 (2H, d,  $J=8.8\text{Hz}$ ), 8.0-8.4 (6H, m), 8.85 (1H, s), 8.91 (1H, d,  $J=7.0\text{Hz}$ )

FAB-MASS :  $m/z = 1328$  ( $M+\text{Na}$ ) $^+$

Elemental Analysis Calcd. for  $\text{C}_{55}\text{H}_{68}\text{N}_{11}\text{O}_{21}\text{S}_2\text{Na}\cdot 8\text{H}_2\text{O}$  :

C 45.55, H 5.84, N 10.62

Found : C 45.62, H 5.70, N 10.54

Example 117

IR (KBr) : 3350, 2939, 1664, 1627, 1531, 1446, 1249, 1049  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.8-1.0 (6H, m), 1.4-1.9 (9H, m), 2.0-2.5 (4H, m), 3.1-3.2 (1H, m), 3.22 (3H, s), 3.3-3.4 (2H, m), 3.51 (2H, s), 3.6-4.4 (16H, m), 4.7-5.2 (7H, m), 5.07 (1H, d,  $J=5.6\text{Hz}$ ), 5.17 (1H, d,  $J=3.1\text{Hz}$ ), 5.23 (1H, d,  $J=4.5\text{Hz}$ ), 5.54 (1H, d,  $J=5.9\text{Hz}$ ), 6.7-6.8 (3H, m), 7.0-7.4 (8H, m), 7.5-7.7 (4H, m), 7.70 (4H, s), 8.1-8.2 (2H, m), 8.51 (1H, d,  $J=7.0\text{Hz}$ ), 8.83 (1H, s)

FAB-MASS :  $m/z = 1367.6$  ( $M+\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{61}\text{H}_{77}\text{N}_8\text{O}_{23}\text{SNa}\cdot 6.5\text{H}_2\text{O}$  :

C 50.01, H 6.20, N 7.66

Found : C 50.30, H 6.50, N 7.75

Example 118

To a solution of The Object Compound (61) (0.25 g) in methanol (50 ml) was added dry 10% palladium on carbon (0.2 g) and stirred for 6 hours under hydrogen atmosphere. The palladium on carbon was filtered off, and the filtrate was

246

evaporated under reduced pressure to give Object Compound 118 (179 mg).

IR (KBr) : 3400, 1668.1, 1627.6  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.92 (3H, d,  $J=6.7\text{Hz}$ ), 1.1-2.45 (40H, m), 3.20 (3H, s), 3.28 (2H, t,  $J=6.5\text{Hz}$ ), 3.0-3.4 (1H, m), 3.5-4.7 (14H, m), 4.95-5.5 (12H, m), 6.55 (1H, d,  $J=8.4\text{Hz}$ ), 6.84 (1H, s), 6.86 (1H, d,  $J=8.4\text{Hz}$ ), 7.0-7.3 (4H, m), 7.9-8.3 (4H, m)

FAB-MASS :  $m/z = 1292$  (M+Na)

Elemental Analysis Calcd. for  $\text{C}_{54}\text{H}_{88}\text{N}_9\text{O}_{22}\text{SNa}\cdot 5\text{H}_2\text{O}$  :

C 47.67, H 7.26, N 9.26

Found : C 47.72, H 7.35, N 8.95

The Object Compounds (119) to (121) were obtained according to a similar manner to that of Example 118.

#### Example 119

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.6\text{Hz}$ ), 1.00 (3H, d,  $J=7.3\text{Hz}$ ), 1.03 (3H, d,  $J=6.0\text{Hz}$ ), 1.2-1.5 (4H, m), 1.5-2.0 (5H, m), 2.1-2.7 (8H, m), 3.17 (1H, m), 3.6-4.5 (14H, m), 4.65-5.7 (12H, m), 6.72 (1H, d,  $J=8.1\text{Hz}$ ), 6.75 (1H, s), 6.80 (1H, d,  $J=8.1\text{Hz}$ ), 7.05 (1H, s), 7.1-7.7 (15H, m), 8.0-8.6 (4H, m), 8.85 (1H, s)

FAB-MASS :  $m/z = 1274$  (M+Na)

Elemental Analysis Calcd. for  $\text{C}_{55}\text{H}_{74}\text{N}_9\text{O}_{21}\text{SNa}\cdot 7\text{H}_2\text{O}$  :

C 47.93, N 6.43, N 9.15

Found : C 48.12, N 6.56, N 9.03

#### Example 120

IR (KBr) : 3355.5, 1672.0 1629.6  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.6\text{Hz}$ ), 0.98 (3H, d,  $J=6.5\text{Hz}$ ), 1.03 (3H, d,  $J=6.0\text{Hz}$ ), 1.2-2.6 (21H, m), 3.18 (1H, m), 3.6-4.5 (16H, m), 4.65-5.55 (12H, m), 6.6-7.5 (10H, m), 8.0-8.6 (4H, m), 8.89 (1H, s)

247

FAB-MASS :  $m/z = 1256$  (M+Na)

Example 121

IR (KBr) : 3357.5, 1660.4, 1629.6, 1249.6  $\text{cm}^{-1}$

5 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.6\text{Hz}$ ), 0.96 (3H, d,  $J=6.8\text{Hz}$ ), 1.03 (3H, d,  $J=6.0\text{Hz}$ ), 1.1-1.5 (12H, m), 1.6-2.0 (5H, m), 2.0-2.5 (4H, m), 3.07 (1H, m), 3.5-4.5 (16H, m), 4.6-5.6 (12H, m), 6.72 (1H, d,  $J=8.1\text{Hz}$ ), 6.7-6.9 (4H, m), 7.04 (1H, s), 7.16 (1H, s), 7.1-7.5 (2H, m), 7.25 (2H, d,  $J=8.6\text{Hz}$ ), 8.0-8.2 (3H, m), 8.46 (1H, d,  $J=7\text{Hz}$ ), 8.84 (1H, s)

10 FAB-MASS :  $m/z = 1256$  (M+Na)

Elemental Analysis Calcd. for  $\text{C}_{52}\text{H}_{76}\text{N}_9\text{O}_{22}\text{SNa}\cdot 7\text{H}_2\text{O}$  :

C 45.91, H 6.67, N 9.27

15 Found : C 45.98, H 6.67, N 9.10

Example 122

A solution of Object Compound (11) (795 mg) in water (16 ml) was left for 240 hours. The solution was subjected to column chromatography on ODS (YMC-gel ODS-AMS50) and eluted with 25%  $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ . The fractions containing Object Compound were combined and the acetonitrile was removed under reduced pressure. The residue was lyophilized to give Object Compound (123) (38 mg).

25 IR (KBr) : 3361, 2956, 2875, 1668, 1627, 1521, 1249, 1047  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.8-1.5 (19H, m), 1.6-2.4 (13H, m), 3.1-3.2 (1H, m), 3.5-4.1 (12H, m), 4.1-4.7 (10H, m), 4.9-5.6 (5H, m), 5.98 (1H, d,  $J=10.6\text{Hz}$ ), 6.36 (1H, d,  $J=10.6\text{Hz}$ ), 6.7-7.3 (12H, m), 7.4-8.0 (7H, m)

30 FAB-MASS :  $m/z = 1273.1$  (M+Na<sup>+</sup>)

Elemental Analysis Calcd. for  $\text{C}_{55}\text{H}_{71}\text{N}_8\text{O}_{22}\text{NaS}\cdot 11\text{H}_2\text{O}$  :

C 45.58, H 6.47, N 7.73

35 Found : C 45.83, H 6.26, N 7.75

08809723.052197  
261250" E260880

248

The Object Compound (123) was obtained according to a similar manner to that of Example 118.

Example 123

5 IR (KBr) : 3349.7, 1670.1, 1627.6  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=7.2\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.13 (3H, d,  $J=5.7\text{Hz}$ ), 1.18-1.55 (10H, m), 1.58-2.08 (5H, m), 2.08-2.90 (4H, m), 2.90-3.30 (2H, m), 3.60-4.50 (17H, m), 4.70-5.70 (12H, m),  
10 6.65-7.60 (11H, m), 7.80 (2H, br s), 7.95-8.23 (2H, m), 8.75 (1H, d,  $J=7.0\text{Hz}$ ), 8.85 (1H, s)  
FAB-MASS :  $m/z = 1114.4$  ( $\text{M}-\text{SO}_4-2$ )  
Elemental Analysis Calcd. for  $\text{C}_{52}\text{H}_{77}\text{N}_9\text{O}_{21}\text{S}\cdot 6\text{H}_2\text{O}$  :  
C 47.88, H 6.88, N 9.66  
15 Found : C 47.60, H 6.74, N 9.53

The following compound (124) was obtained according to a similar manner to that of Example 1.

Example 124

20 IR (KBr) : 3324, 2937, 2873, 1664, 1629, 1442, 1257  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.91 (3H, t,  $J=7.1\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.09 (3H, d,  $J=5.7\text{Hz}$ ), 1.3-1.5 (4H, m),  
25 1.7-2.6 (9H, m), 3.1-3.3 (1H, m), 3.7-4.6 (16H, m), 4.7-5.1 (7H, m), 5.11 (1H, d,  $J=5.6\text{Hz}$ ), 5.17 (1H, d,  $J=3.1\text{Hz}$ ), 5.26 (1H, d,  $J=4.5\text{Hz}$ ), 5.55 (1H, d,  $J=5.8\text{Hz}$ ), 6.7-6.9 (3H, m), 7.0-7.6 (6H, m), 7.97 (2H, d,  $J=8.8\text{Hz}$ ), 8.0-8.4 (6H, m), 8.85 (1H, s),  
30 8.92 (1H, d,  $J=7.0\text{Hz}$ )

FAB-MASS :  $m/z = 1331$  ( $\text{M}+\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{55}\text{H}_{69}\text{N}_{10}\text{O}_{22}\text{NaS}_2$  :  
C 45.45, H 5.89, N 9.64  
35 Found : C 45.71, H 5.68, N 9.60

249